

=> fil hcap
FILE 'HCAPLUS' ENTERED AT 12:54:04 ON 16 MAR 2005
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FILE COVERS 1907 - 16 Mar 2005 VOL 142 ISS 12
FILE LAST UPDATED: 15 Mar 2005 (20050315/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil reg
FILE 'REGISTRY' ENTERED AT 12:54:07 ON 16 MAR 2005
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 15 MAR 2005 HIGHEST RN 845699-17-4
DICTIONARY FILE UPDATES: 15 MAR 2005 HIGHEST RN 845699-17-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> => d que 160
L56 (1)SEA FILE=HCAPLUS ABB=ON PLU=ON US2003-729387/APPS
L57 SEL PLU=ON L56 1- RN : 6 TERMS
L58 6 SEA FILE=REGISTRY ABB=ON PLU=ON L57
L59 127705 SEA FILE=REGISTRY ABB=ON PLU=ON ?DIOXOLAN?/CNS
L60 2 SEA FILE=REGISTRY ABB=ON PLU=ON L58 AND L59

=> d ide 160 1-2

L60 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN 145918-75-8 REGISTRY

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2(1H)-Pyrimidinone, 4-amino-1-[2-(hydroxymethyl)-1,3-dioxolan-4-yl]-, (2S-cis)-

OTHER NAMES:

CN (-)-BCH 204

CN (-)-OccC

CN BCH 4556

CN L-OddC

CN SPD 758

CN Troxacitabine

CN Troxatyl

FS STEREOSEARCH

MF C8 H11 N3 O4

CI COM

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMINFORMRX, CIN, EMBASE, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

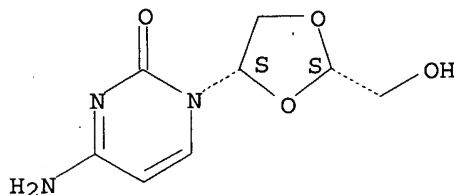
DT.CA CAPLUS document type: Dissertation; Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

78 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

80 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L60 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN

RN 145397-26-8 REGISTRY

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[2-(hydroxymethyl)-1,3-dioxolan-4-yl]-, (2S-cis)-

FS STEREOSEARCH

MF C8 H10 F N3 O4

SR CA

LC STN Files: CA, CAPLUS, CHEMINFORMRX, MEDLINE, PROUSDDR, SYNTHLINE,

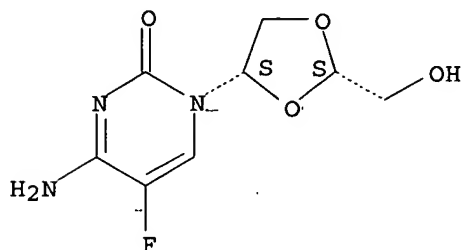
TOXCENTER, USPAT2, USPATFULL

DT.CA CAPlus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1907 TO DATE)

11 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d que l3

L3 2 SEA FILE=REGISTRY ABB=ON PLU=ON 220127-57-1/RN,CRN

=> d ide l3 1-2

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN

RN 790208-79-6 REGISTRY

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate, mixt. with 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]-2(1H)-pyrimidinone (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C29 H31 N7 O . C8 H11 N3 O4 . C H4 O3 S

CI MXS

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

DT.CA CAPlus document type: Patent

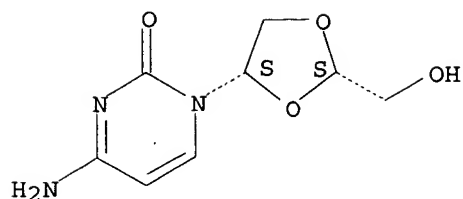
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

CM 1

CRN 145918-75-8

CMF C8 H11 N3 O4

Absolute stereochemistry. Rotation (-).



CM 2

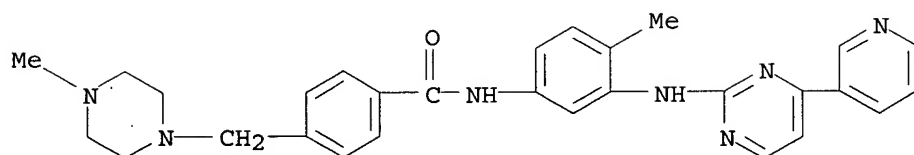
CRN 220127-57-1

CMF C29 H31 N7 O . C H4 O3 S

CM 3

CRN 152459-95-5

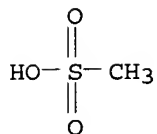
CMF C29 H31 N7 O



CM 4

CRN 75-75-2

CMF C H4 O3 S



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN

RN 220127-57-1 REGISTRY

CN Benzamide, 4-[[4-methyl-1-piperazinyl]methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

OTHER NAMES:

CN CGP 57148B

CN Gleevac

CN Gleevec

CN Glivec

CN Imatinib mesilate

CN Imatinib mesylate

CN STI 571

MF C29 H31 N7 O . C H4 O3 S

CI COM

SR CA

LC STN Files: ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, EMBASE, HSDB*, IMSPATENTS, IMSRESEARCH, MRCK*, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL

(*File contains numerically searchable property data)

DT.CA Caplus document type: Conference; Dissertation; Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

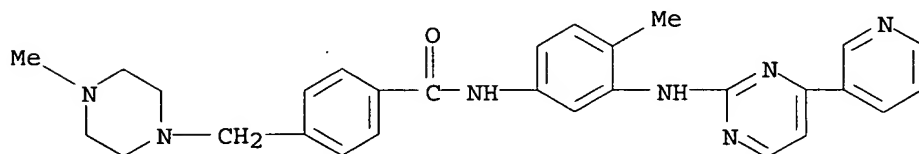
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties)

CM 1

CRN 152459-95-5

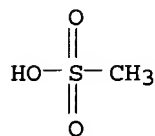
CMF C29 H31 N7 O



CM 2

CRN 75-75-2

CMF C H4 O3 S



857 REFERENCES IN FILE CA (1907 TO DATE)

8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

863 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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FILE COVERS 1907 - 16 Mar 2005 VOL 142 ISS 12
FILE LAST UPDATED: 15 Mar 2005 (20050315/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil medlin
FILE 'MEDLINE' ENTERED AT 13:21:25 ON 16 MAR 2005

FILE LAST UPDATED: 15 MAR 2005 (20050315/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil biosis
FILE 'BIOSIS' ENTERED AT 13:21:28 ON 16 MAR 2005
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNS) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 9 March 2005 (20050309/ED)

FILE RELOADED: 19 October 2003.

=> fil embase
FILE 'EMBASE' ENTERED AT 13:21:30 ON 16 MAR 2005
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FILE COVERS 1974 TO 10 Mar 2005 (20050310/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil drugu

FILE 'DRUGU' ENTERED AT 13:21:33 ON 16 MAR 2005

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FILE LAST UPDATED: 10 MAR 2005 <20050310/UP>

>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<

>>> THESAURUS AVAILABLE IN /CT <<<

>>> A RECENT REVIEW OF PSYCHIATRIC DISEASE KEYWORDS USED
IN DERWENT DRUG FILE HAS PROMPTED A REVISION BASED
ON STANDARD TERMS USED IN DSM-IV (DIAGNOSTIC AND
STATISTICAL MANUAL OF MENTAL DISORDERS - FOURTH
EDITION).

FOR FURTHER DETAILS:

http://thomsonderwent.com/derwenthome/support/userguides/lit_guide

=> fil wpix

FILE 'WPIX' ENTERED AT 13:21:37 ON 16 MAR 2005

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FILE LAST UPDATED: 11 MAR 2005 <20050311/UP>

MOST RECENT DERWENT UPDATE: 200517 <200517/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:

http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE

<http://thomsonderwent.com/coverage/latestupdates/> <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
GUIDES, PLEASE VISIT:

<http://thomsonderwent.com/support/userguides/> <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
FIRST VIEW - FILE WPIFV.

FOR FURTHER DETAILS: <http://www.thomsonderwent.com/dwpifv> <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.

PLEASE CHECK:

<http://thomsonderwent.com/support/dwpioref/reftools/classification/code-revision/>
FOR DETAILS. <<<

=> fil pascal

FILE 'PASCAL' ENTERED AT 13:21:41 ON 16 MAR 2005

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FILE LAST UPDATED: 14 MAR 2005 <20050314/UP>
FILE COVERS 1977 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION IS AVAILABLE
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=> fil jicst
FILE 'JICST-EPLUS' ENTERED AT 13:21:45 ON 16 MAR 2005
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FILE COVERS 1985 TO 14 MAR 2005 (20050314/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED
TERM (/CT) THESAURUS RELOAD.

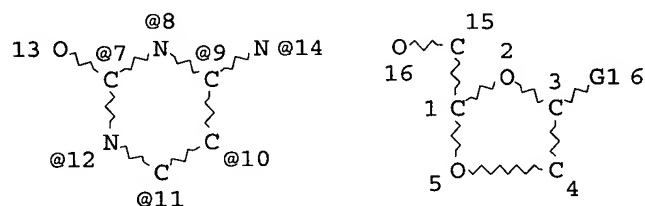
=> fil scisearch
FILE 'SCISEARCH' ENTERED AT 13:21:49 ON 16 MAR 2005
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FILE COVERS 1974 TO 10 Mar 2005 (20050310/ED)

=> file stnguide
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 11, 2005 (20050311/UP).

=> d que 116
L4 STR



VAR G1=7/8/9/14/10/11/12
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L5 (452)SEA FILE=REGISTRY SSS FUL L4
L6 (2)SEA FILE=REGISTRY ABB=ON PLU=ON 220127-57-1/RN,CRN
L7 (116)SEA FILE=HCAPLUS ABB=ON PLU=ON L5
L8 (863)SEA FILE=HCAPLUS ABB=ON PLU=ON L6
L9 (11)SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND L8

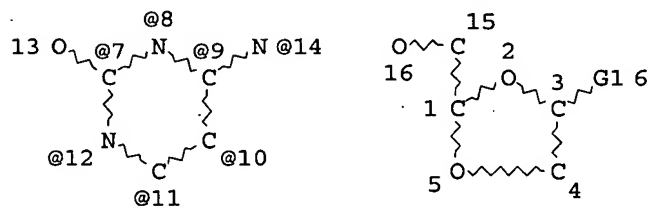
```

L10      QUE ABB=ON PLU=ON (?TYROSIN?(2A)?KINAS?) (3A) (?INHIBI
        T? OR ?RUPT? OR ?BLOCK? OR ?MODERAT? OR ?MODULAT?)
L11      QUE ABB=ON PLU=ON ?IMATINIB? (2A) ?MESYL?
L12      QUE ABB=ON PLU=ON STI(1W)571
L13 (    8)SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND ((L10 OR L11 OR L12))
L14      QUE ABB=ON PLU=ON ?TYROSIN?(2A)?KINAS?
L15 (    5)SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND L14
L16      12 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 OR L13 OR L15

```

=> d que l33

L1 STR



```

VAR G1=7/8/9/14/10/11/12
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

```

```

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

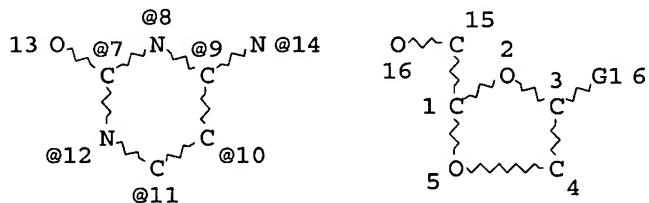
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STEREO ATTRIBUTES: NONE

```

L2      452 SEA FILE=REGISTRY SSS FUL L1
L11     QUE ABB=ON PLU=ON ?IMATINIB? (2A) ?MESYL?
L12     QUE ABB=ON PLU=ON STI(1W)571
L14     QUE ABB=ON PLU=ON ?TYROSIN?(2A)?KINAS?
L19     STR

```



```

VAR G1=7/8/9/14/10/11/12
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

```

```

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

```

STEREO ATTRIBUTES: NONE

```

L20 (    452)SEA FILE=REGISTRY SSS FUL L19
L21 (    2)SEA FILE=REGISTRY ABB=ON PLU=ON 220127-57-1/RN,CRN
L22     SEL. PLU=ON L20 1- CHEM :      474 TERMS

```

L23 (86) SEA FILE=MEDLINE ABB=ON PLU=ON L22
L24 SEL PLU=ON L21 1- CHEM : 9 TERMS
L25 (1112) SEA FILE=MEDLINE ABB=ON PLU=ON L24
L26 9 SEA FILE=MEDLINE ABB=ON PLU=ON L23 AND L25
L30 SEL PLU=ON L2 1- CHEM : 474 TERMS
L31 86 SEA FILE=MEDLINE ABB=ON PLU=ON L30
L32 9 SEA FILE=MEDLINE ABB=ON PLU=ON L31 AND (L11 OR L12 OR L14)
L33 10 SEA FILE=MEDLINE ABB=ON PLU=ON L32 OR L26

=> d que nos 140

L1 STR
L2 452 SEA FILE=REGISTRY SSS FUL L1
L3 2 SEA FILE=REGISTRY ABB=ON PLU=ON 220127-57-1/RN,CRN
L11 QUE ABB=ON PLU=ON ?IMATINIB? (2A) ?MESYL?
L12 QUE ABB=ON PLU=ON STI(1W)571
L14 QUE ABB=ON PLU=ON ?TYROSIN?(2A)?KINAS?
L34 SEL PLU=ON L2 1- CHEM : 474 TERMS
L35 125 SEA FILE=EMBASE ABB=ON PLU=ON L34
L36 SEL PLU=ON L3 1- CHEM : 9 TERMS
L37 3491 SEA FILE=EMBASE ABB=ON PLU=ON L36
L38 24 SEA FILE=EMBASE ABB=ON PLU=ON L35 AND L37
L39 20 SEA FILE=EMBASE ABB=ON PLU=ON L35 AND (L14 OR L11 OR L12)
L40 27 SEA FILE=EMBASE ABB=ON PLU=ON L38 OR L39

=> d que nos 148

L1 STR
L2 452 SEA FILE=REGISTRY SSS FUL L1
L3 2 SEA FILE=REGISTRY ABB=ON PLU=ON 220127-57-1/RN,CRN
L12 QUE ABB=ON PLU=ON STI(1W)571
L14 QUE ABB=ON PLU=ON ?TYROSIN?(2A)?KINAS?
L41 QUE ABB=ON PLU=ON ?IMATINIB?
L42 SEL PLU=ON L2 1- CHEM : 474 TERMS
L43 98 SEA FILE=BIOSIS ABB=ON PLU=ON L42
L44 SEL PLU=ON L3 1- CHEM : 9 TERMS
L45 1470 SEA FILE=BIOSIS ABB=ON PLU=ON L44
L46 5 SEA FILE=BIOSIS ABB=ON PLU=ON L43 AND L45
L47 4 SEA FILE=BIOSIS ABB=ON PLU=ON L43 AND (L41 OR L14 OR L12)
L48 5 SEA FILE=BIOSIS ABB=ON PLU=ON L46 OR L47

=> d que nos 155

L1 STR
L2 452 SEA FILE=REGISTRY SSS FUL L1
L3 2 SEA FILE=REGISTRY ABB=ON PLU=ON 220127-57-1/RN,CRN
L12 QUE ABB=ON PLU=ON STI(1W)571
L14 QUE ABB=ON PLU=ON ?TYROSIN?(2A)?KINAS?
L41 QUE ABB=ON PLU=ON ?IMATINIB?
L49 SEL PLU=ON L2 1- CHEM : 474 TERMS
L50 104 SEA FILE=DRUGU ABB=ON PLU=ON L49
L51 SEL PLU=ON L3 1- CHEM : 9 TERMS
L52 1077 SEA FILE=DRUGU ABB=ON PLU=ON L51
L53 7 SEA FILE=DRUGU ABB=ON PLU=ON L50 AND L52
L54 8 SEA FILE=DRUGU ABB=ON PLU=ON L50 AND (L14 OR L41 OR L12)
L55 9 SEA FILE=DRUGU ABB=ON PLU=ON L53 OR L54

=> d que 178

L64 12 SEA FILE=WPIX ABB=ON PLU=ON ((?TROXACITABIN?/BIX OR ?TROXATYL

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                ?/BIX OR (SPD/BIX(1W)758/BIX) OR OCCC/BIX OR (BCH/BIX(1W)(204/B
                IX OR 4556/BIX)) OR (?DIOXALAN?/BIX(1W)C/BIX)))
L65          48 SEA FILE=WPIX ABB=ON PLU=ON (((CGP/BIX(1W)57148B/BIX) OR
                ?GLEEVAC?/BIX OR ?GLEEVEC?/BIX OR ?GLIVEC?/BIX))
L66          2131 SEA FILE=WPIX ABB=ON PLU=ON (?TYROSIN?/BIX(2A)?KINAS?/BIX)
L67          77 SEA FILE=WPIX ABB=ON PLU=ON (?IMATINIB?/BIX)
L68          16 SEA FILE=WPIX ABB=ON PLU=ON (STI/BIX(1W)571/BIX)
L69          6 SEA FILE=WPIX ABB=ON PLU=ON L64 AND (L65 OR L66 OR L67 OR
                L68)
L70          13221 SEA FILE=WPIX ABB=ON PLU=ON (B14-S09 OR C14-S09 OR B12-C09
                OR C12-C09)/MC
L71          2 SEA FILE=WPIX ABB=ON PLU=ON L64 AND L70
L72          2 SEA FILE=WPIX ABB=ON PLU=ON L65 AND L70
L73          11 SEA FILE=WPIX ABB=ON PLU=ON L67 AND L70
L74          11 SEA FILE=WPIX ABB=ON PLU=ON (L71 OR L72 OR L73)
L75          18409 SEA FILE=WPIX ABB=ON PLU=ON A61P035?/IPC
L76          57371 SEA FILE=WPIX ABB=ON PLU=ON (B14-H? OR C14-H?)/MC
L77          11 SEA FILE=WPIX ABB=ON PLU=ON L74 AND (L75 OR L76)
L78          15 SEA FILE=WPIX ABB=ON PLU=ON L69 OR L77

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=> d his 182

```

(FILE 'PASCAL, JICST-EPLUS, SCISEARCH' ENTERED AT 13:11:56 ON 16 MAR 2005)
L82          6 DUP REM L81 (4 DUPLICATES REMOVED)

```

=> d que 182

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L12          QUE ABB=ON PLU=ON STI(1W)571
L14          QUE ABB=ON PLU=ON ?TYROSIN?(2A)?KINAS?
L41          QUE ABB=ON PLU=ON ?IMATINIB?
L62          QUE ABB=ON PLU=ON (?TROXACITABIN? OR ?TROXATYL? OR (SP
                D(1W)758) OR OCCC OR (BCH(1W)(204 OR 4556)) OR (?DIOXALAN
                ?(1W)C))
L63          QUE ABB=ON PLU=ON ((CGP(1W)57148B) OR ?GLEEVAC? OR ?GL
                EEVEC? OR ?GLIVEC?)
L79          134 SEA L62
L80          65582 SEA (L63 OR L12 OR L41 OR L14)
L81          10 SEA L79 AND L80
L82          6 DUP REM L81 (4 DUPLICATES REMOVED)

```

=> dup rem 116 133 140 148 155 178 182

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PROCESSING COMPLETED FOR L40
PROCESSING COMPLETED FOR L48
PROCESSING COMPLETED FOR L55
PROCESSING COMPLETED FOR L78
PROCESSING COMPLETED FOR L82
L89 54 DUP REM L16 L33 L40 L48 L55 L78 L82 (30 DUPLICATES REMOVED)
 ANSWERS '1-12' FROM FILE HCAPLUS
 ANSWERS '13-18' FROM FILE MEDLINE
 ANSWERS '19-37' FROM FILE EMBASE
 ANSWER '38' FROM FILE BIOSIS
 ANSWERS '39-45' FROM FILE DRUGU
 ANSWERS '46-54' FROM FILE WPIX

=> file stnguide

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LAST RELOADED: Mar 11, 2005 (20050311/UP).

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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' -
CONTINUE? (Y)/N:y

L89 ANSWER 1 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2004:1036851 HCAPLUS

DOCUMENT NUMBER: 142:696

TITLE: Synergistic treatment of cancer using immunomers in
conjunction with chemotherapeutic agents

INVENTOR(S): Kandimalla, Ekambar R.; Agrawal, Sudhir; Wang, Daqin

PATENT ASSIGNEE(S): Hybridon, Inc., USA

SOURCE: PCT Int. Appl., 106 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103301	A2	20041202	WO 2004-US15313	20040514
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2005009773 A1 20050113 US 2004-846167 20040514

PRIORITY APPLN. INFO.: US 2003-471247P P 20030516

OTHER SOURCE(S): MARPAT 142:696

ED Entered STN: 03 Dec 2004

AB The invention discloses the therapeutic use of immunostimulatory oligonucleotides and/or immunomers in combination with chemotherapeutic agents to provide a synergistic therapeutic effect.

IT 145918-75-8, BCH-4556

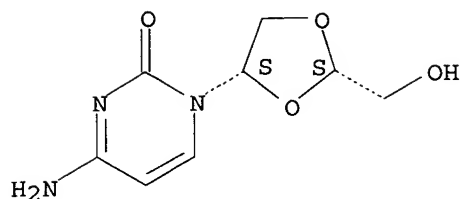
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(immunostimulatory oligonucleotide and/or immunomer combination with chemotherapeutic agent for synergistic cancer treatment)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IC ICM A61K
 CC 1-6 (Pharmacology)
 IT 50-07-7, Mitomycin C 50-44-2, Mercaptopurine 50-76-0, Dactinomycin
 50-91-9, Floxuridine 51-21-8, 5-Fluorouracil 52-24-4, Thiotepa
 53-19-0, Mitotane 55-86-7, Mechlorethamine hydrochloride 55-98-1,
 Busulfan 57-22-7, Vincristine 59-05-2, Methotrexate 69-74-9,
 Cytarabine hydrochloride 125-84-8, Aminoglutethimide 127-07-1,
 Hydroxyurea 143-67-9, Vinblastine sulfate 145-63-1, Suramin
 147-94-4, DepoCyt 148-82-3, Melphalan 154-93-8, Carmustine
 305-03-3, Chlorambucil 320-67-2, Azacitidine 366-70-1, Procarbazine
 hydrochloride 459-86-9, Mitoguazone 645-05-6, Hexamethylmelamine
 3094-09-5, Furtulon 3778-73-2 4291-63-8, Leustatin 4342-03-4,
 Dacarbazine 9015-68-3, Asparaginase 11056-06-7, Bleomycin
 11096-26-7, Erythropoietin 13010-20-3D, Nitrosourea, derivs.
 13010-47-4, Lomustine 13311-84-7, Flutamide 13909-09-6, Semustine
 14769-73-4, Levamisole 15663-27-1, Cisplatin 16595-80-5, Ergamisol
 18378-89-7, Plicamycin 18883-66-4, Streptozocin 19764-02-4, Fragilin
 19767-45-4, Mesna 23214-92-8, Evacet 23541-50-6, Daunorubicin
 hydrochloride 25316-40-9, Adriamycin 29767-20-2, Vumon 33069-62-4,
 Yewtaxan 33419-42-0 38270-90-5, Metastron 38819-10-2D,
 Guaninearabinoside, prodrug derivative 39325-01-4, Picibanil 41575-94-4,
 Paraplatin 51264-14-3, Amsacrine 52205-73-9, Estramustine phosphate
 sodium 53910-25-1, 2'Deoxycoformycin 54965-24-1, Tamoxifen citrate
 56124-62-0, Valrubicin 56420-45-2, Pharmarubicin 59917-39-4, Vindesine
 sulfate 59989-18-3, Eniluracil 65271-80-9, Novantrone 66849-34-1, D
 4809 70476-82-3, Mitoxantrone hydrochloride 74381-53-6, Leuprolide
 acetate 74578-38-4, Uft 75607-67-9, Fludara 83150-76-9, Octreotide
 85622-93-1, Temodal 90409-78-2, Polifeprosan 91421-43-1,
 9-Aminocamptothecin 95058-81-4, Gemcitabine 97682-44-5, Camptosar
 100286-90-6, Campto 102409-92-7, FK 317 106400-81-1, LY 264618
 112522-64-2, CI-994 112887-68-0, Tomudex 114977-28-5, Taxotere
 119876-18-5D, non-sugar-containing derivs. 120685-11-2, PKC412
 121584-18-7, Valspodar 122111-03-9, Gemzar 123948-87-8, Topotecan
 129298-91-5, TNP-470 129580-63-8, BMS 182751 130370-60-4, Batimastat
 141907-41-7 **145918-75-8**, BCH-4556 146426-40-6, HMR 1275
 150399-23-8, LY231514 151823-14-2, CS-682 153537-73-6, ZD 9331
 154039-60-8, TA 2516 154361-50-9, Xeloda 159776-69-9, LU.103793
 159997-94-1, Incel 162706-37-8, LU 79553 165668-41-7, E7070
 169799-04-6, MMI270 169869-90-3, DX8951 f 174722-31-7, Rituxan
 179545-77-8, BAY 12-9566 180288-69-1, Herceptin 181630-15-9, ZD 0473
 183012-14-8, YM 116 183319-69-9, CP 358774 184046-91-1 184475-35-2,
 ZD1839 190454-58-1, VX 853 192329-42-3, AG3340 209164-46-5, CDP 845
220127-57-1, Gleevec 259188-38-0, D2163 289499-45-2, PD183805
 386211-12-7, AG 3433 386211-13-8, ZD 0101 386211-20-7, ISI 641
 386211-21-8, ODN 698 386211-47-8, Lemonal DP 2202 386211-48-9, CP
 609754 799292-77-6, Glamolec
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (immunostimulatory oligonucleotide and/or immunomer combination with
 chemotherapeutic agent for synergistic cancer treatment)

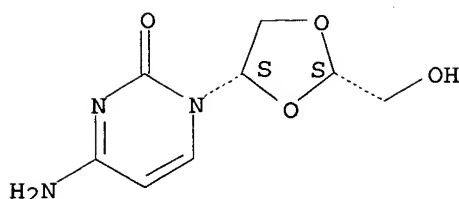
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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' -
CONTINUE? (Y)/N:y

L89 ANSWER 2 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:965080 HCAPLUS
DOCUMENT NUMBER: 141:388665
TITLE: Method for infusion administration of troxacitabine
for the treatment of cancer
INVENTOR(S): Jolivet, Jacques; Gourdeau, Henriette
PATENT ASSIGNEE(S): Shire Biochem Inc., Can.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096239	A1	20041111	WO 2004-CA446	20040324
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004248915	A1	20041209	US 2004-806336	20040323
PRIORITY APPLN. INFO.:			US 2003-465228P	P 20030425
ED	Entered STN:	12 Nov 2004		
AB	In the treatment of cancer, troxacitabine or a pharmaceutically acceptable salt can be effectively administered to a host having a tumor by continuous infusion for a period of at least 72 h, wherein the amount is sufficient to provide tumor reduction			
IT	145918-75-8, Troxacitabine RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (troxacitabine infusion for treatment of cancer)			
RN	145918-75-8 HCAPLUS			
CN	2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)			

Absolute stereochemistry. Rotation (-).



IC ICM A61K031-704
ICS A61P035-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 63
IT 145918-75-8, Troxacitabine
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(troxacitabine infusion for treatment of cancer)
IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-44-2, Mercaptopurine 51-75-2, Mechlorethamine 53-03-2, Prednisone 55-98-1, Busulfan 57-22-7, Vincristine 59-05-2, Methotrexate 127-07-1, Hydroxyurea 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7, 6-Thioguanine 154-93-8, Carmustine 302-79-4, Retinoic acid 305-03-3, Chlorambucil 671-16-9, Procarbazine 865-21-4, Vinblastine 1404-00-8, Mitomycin 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4342-03-4, Dacarbazine 9014-42-0, Thrombopoietin 9015-68-3, Asparaginase 11056-06-7, Bleomycin 11096-26-7, Epoetin 13010-47-4, Lomustine 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 23214-92-8, Doxorubicin 33419-42-0, Etoposide 53910-25-1, Pentostatin 58957-92-9, Idarubicin 62683-29-8, Colony-stimulating factor 65271-80-9, Mitoxantrone 83869-56-1, GM-CSF 95058-81-4, Gemcitabine 121181-53-1, Filgrastim 121584-18-7, PSC 833 123774-72-1, Sargramostim 123948-87-8, Topotecan 143011-72-7, G-CSF 174722-31-7, Rituxan 220127-57-1, Gleeevec 220578-59-6, CMA-676 790208-65-0
790208-66-1 790208-67-2 790208-68-3
790208-69-4 790208-70-7 790208-71-8
790208-72-9 790208-73-0 790208-74-1
790208-75-2 790208-76-3 790208-77-4
790208-78-5 790208-79-6 790208-80-9
790208-81-0 790208-82-1 790208-83-2
790208-84-3 790208-85-4 790208-86-5
790208-87-6 790208-88-7 790208-89-8
790208-90-1 790208-91-2 790208-92-3
790208-93-4 790208-94-5 790208-95-6
790208-96-7 790208-97-8 790208-98-9
790208-99-0 790209-00-6 790209-01-7
790209-02-8 790209-03-9 790209-04-0
790209-05-1 790209-06-2 790209-07-3
790209-08-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(troxacitabine infusion for treatment of cancer, and use with other agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 3 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:513542 HCAPLUS
DOCUMENT NUMBER: 141:47311

TITLE: Pharmaceutical combinations and methods using dioxolanyl cytosine derivatives and dioxolanyl 5-fluorocytosine derivatives for the treatment of leukemia

INVENTOR(S): Giles, Francis J.; Verstovsek, Srdan

PATENT ASSIGNEE(S): Shire Biochem Inc., Can.

SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052369	A1	20040624	WO 2003-CA1909	20031208
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004192652	A1	20040930	US 2003-729387	20031208
PRIORITY APPLN. INFO.:			US 2002-431196P	P 20021206

OTHER SOURCE(S): MARPAT 141:47311

ED Entered STN: 25 Jun 2004

AB The invention provides a pharmaceutical combination useful for the treatment of leukemia comprising at least one cytosine or 5-fluorocytosine derivative and a Bcr-Abl **tyrosine kinase inhibitor**, as well as a method of treating a patient having leukemia comprising at least one cytosine or 5-fluorocytosine derivative and a Bcr-Abl **tyrosine kinase inhibitor**.

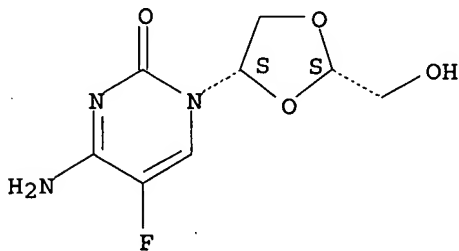
IT 145397-26-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dioxolanyl cytosine derivs. and dioxolanyl 5-fluorocytosine derivs. for treatment of leukemia)

RN 145397-26-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-5-fluoro-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IC ICM A61K031-506

ICS A61K031-513; A61P035-00; A61P035-02

CC 1-6 (Pharmacology)
 ST cytosine dioxolanyl deriv Bcr Abl **tyrosine kinase inhibitor** leukemia; fluorocytosine dioxolanyl deriv Bcr Abl **tyrosine kinase inhibitor** leukemia
 IT 138238-67-2, Bcr-Abl **tyrosine kinase**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (dioxolanyl cytosine derivs. and dioxolanyl 5-fluorocytosine derivs. for treatment of leukemia)
 IT 71-30-7D, Cytosine, dioxolanyl derivs. 2022-85-7D, 5-Fluorocytosine, dioxolanyl derivs. 145397-26-8 145918-75-8 220127-57-1, **Imatinib mesylate**
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (dioxolanyl cytosine derivs. and dioxolanyl 5-fluorocytosine derivs. for treatment of leukemia)

L89 ANSWER 4 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2004:453016 HCAPLUS

DOCUMENT NUMBER: 141:1227

TITLE: Combination cancer therapy with a glutathione S-transferase (GST)-activated anticancer compound and another anticancer therapy

INVENTOR(S): Xu, Hua; Brown, Gail L.; Schow, Steven R.; Keck, James G.

PATENT ASSIGNEE(S): Telik, Inc., USA

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045593	A2	20040603	WO 2003-US36209	20031114
WO 2004045593	A3	20040812		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004138140	A1	20040715	US 2003-714593	20031114
			US 2002-426983P	P 20021115

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 141:1227

ED Entered STN: 04 Jun 2004

AB The invention discloses a method for combination cancer therapy in a mammal, especially a human, by administering a therapeutically effective amount of a GST-activated anticancer compound and a therapeutically ED of another anticancer therapy. Also disclosed are pharmaceutical compns., products, and kits for the method, as well as the use of a GST-activated anticancer compound in the manufacture of a medicament for the method. The invention further discloses a method for potentiating an anticancer therapy in a mammal, especially a human, comprising administering a therapeutically effective

amount of a GST-activated anticancer compound to the mammal being treated with the anticancer therapy. Further disclosed is the use of a GST-activated anticancer compound in the manufacture of a medicament for the method. The GST-activated anticancer compound is preferably a compound of US Patent Number 5,556,942, and more preferably TLK286, especially as the hydrochloride salt.

IT 145918-75-8, Troxacitabine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

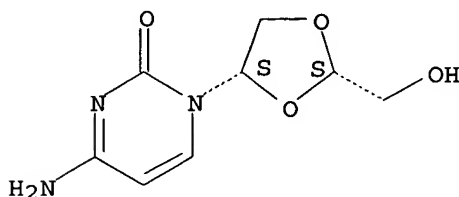
(Biological study); USES (Uses)

(combination cancer therapy with GST-activated anticancer compound and another anticancer therapy)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IC ICM A61K031-00

CC 1-6 (Pharmacology)

Section cross-reference(s): 63

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-35-1, Thalidomide
 50-44-2, Mercaptopurine 50-76-0, Dactinomycin 50-91-9, Floxuridine
 51-21-8, Fluorouracil 51-48-9, Levothyroxine, biological studies
 51-75-2, Mechlorethamine 52-24-4, Thiotepa 53-03-2, Prednisone
 53-19-0, Mitotane 55-98-1, Busulfan 56-53-1, Diethylstilbestrol
 57-22-7, Vincristine 58-05-9, Leucovorin 59-05-2, Methotrexate
 66-75-1, Uramustine 71-58-9, Medroxyprogesteroneacetate 76-43-7,
 Fluoxymesterone 125-84-8, Aminogluthethimide 127-07-1, Hydroxyurea
 145-63-1, Suramin 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7,
 Thioguanine 154-93-8, Carmustine 298-81-7, Methoxsalen 302-79-4,
 trans-Retinoic acid 305-03-3, Chlorambucil 320-67-2, Azacitidine
 566-48-3, Formestane 595-33-5, Megestrol acetate 645-05-6, Altretamine
 671-16-9, Procarbazine 801-52-5, Porfiromycin 865-21-4, Vinblastine
 958-09-8D, chloro derivs. 968-93-4, Testolactone 1327-53-3, Arsenic
 trioxide 1404-00-8, Mitomycin 1605-68-1, Taxane 2098-66-0,
 Cyproterone 2998-57-4, Estramustine 3778-73-2, Ifosfamide 4291-63-8,
 Cladribine 4342-03-4, Dacarbazine 5300-03-8, 9-cis-Retinoic acid
 6893-02-3, Liothyronine 7440-06-4D, Platinum, compds. 9015-68-3,
 L-Asparaginase 9015-68-3D, L-Asparaginase, PEG conjugates 10540-29-1,
 Tamoxifen 11056-06-7, Bleomycin 13010-47-4, Lomustine 13311-84-7,
 Flutamide 13494-90-1, Galliumnitrate 14769-73-4, Levamisole
 15663-27-1, Cisplatin 18378-89-7, Mithramycin 18883-66-4, Streptozocin
 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 23214-92-8,
 Doxorubicin 25322-68-3D, PEG, L-asparaginase conjugates 29767-20-2,
 Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4,
 Carboplatin 51264-14-3, Amsacrine 52128-35-5, Trimetrexate
 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin
 56124-62-0, Valrubicin 56420-45-2, Epirubicin 57773-63-4, Triptorelin
 57982-77-1, Buserelin 58957-92-9, Idarubicin 61825-94-3, Oxaliplatin
 63612-50-0, Nilutamide 65271-80-9, Mitoxantrone 65646-68-6,
 N-(4-Hydroxyphenyl)retinamide 65807-02-5, Goserelin 71486-22-1,
 Vinorelbine 80576-83-6, Edatrexate 83150-76-9, Octreotide

84449-90-1, Raloxifene 85622-93-1, Temozolomide 87806-31-3, Photofrin
 Porfimer sodium 89778-26-7, Toremifene 90357-06-5, Bicalutamide
 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 106685-40-9, Adapalene
 107868-30-4, Exemestane 110942-02-4, Aldesleukin 112809-51-5,
 Letrozole 112887-68-0, Raltitrexed 114977-28-5, Docetaxel
 120511-73-1, Anastrozole 123318-82-1, Clofarabine 123948-87-8,
 Topotecan 129453-61-8, Fulvestrant 129580-63-8, Satraplatin
 137281-23-3, Pemetrexed 145918-75-8, Troxacitabine
 145941-26-0, Oprelvekin 153559-49-0, Bexarotene 154361-50-9,
 Capecitabine 158382-37-7 173146-27-5, Denileukin diftitox
 174722-31-7, Rituximab 179324-69-7, Bortezomib 180288-69-1,
 Trastuzumab 181630-15-9 183319-69-9 184475-35-2, Gefitinib
 192391-48-3 194413-58-6, Semaxanib 205923-56-4, Cetuximab
 206181-63-7 216503-57-0, Alemtuzumab 216974-75-3, Bevacizumab
 220127-57-1, Imatinib mesylate 220578-59-6,
 Gemtuzumab Ozogamicin 439943-59-6, Canglustratide hydrochloride
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(combination cancer therapy with GST-activated anticancer compound and
 another anticancer therapy)

IT 80449-02-1, Protein tyrosine kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; combination cancer therapy with GST-activated
 anticancer compound and another anticancer therapy)

L89 ANSWER 5 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2004:334928 HCAPLUS

DOCUMENT NUMBER: 140:399534

TITLE: Troxacitabine and imatinib mesylate
 combination therapy of chronic myeloid leukaemia:
 preclinical evaluation

AUTHOR(S): Orsolic, Nada; Giles, Francis J.; Gourdeau, Henriette;
 Golemovic, Mirna; Beran, Miloslav; Cortes, Jorge;
 Freireich, Emil J.; Kantarjian, Hagop; Verstovsek,
 Srdan

CORPORATE SOURCE: Department of Leukemia, M.D. Anderson Cancer Center,
 The University of Texas, Houston, TX, USA

SOURCE: British Journal of Haematology (2004), 124(6), 727-738
 CODEN: BJHEAL; ISSN: 0007-1048

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 25 Apr 2004

AB The in vitro and in vivo activity of a deoxycytidine analog,
 troxacitabine, alone or in combination with imatinib
 mesylate (IM), was evaluated against human chronic myeloid
 leukemia (CML) cell lines both sensitive (KBM5 and KBM7) and resistant
 (KBM5-R and KBM7-R) to IM. These cell lines differ in their sensitivity
 to IM but all showed similar sensitivity to treatment with troxacitabine
 (IC₅₀ = 0.5-1 µmol/l). Combined treatment with troxacitabine and IM
 revealed additive or synergistic effects. Greater apoptotic response was
 seen with, combined treatment than with either agent alone in KBM7-R
 cells. In clonogenic assays, troxacitabine showed activity against
 mononuclear cells from CML patients (IC₅₀ = 0.01 µmol/l) with either
 IM-sensitive or resistant disease. In vivo efficacy studies were carried
 out in severe combined immunodeficient mice bearing KBM5 or KBM5-R cells.
 Troxacitabine was administered i.p. daily for 5 d starting on day 20, at
 doses of 5, 10, 20, or 25 mg/kg. IM was administered i.p. twice a day for
 10 d at a dose of 50 mg/kg starting on day 25. In this setting of late
 stage disease, troxacitabine led to a significant increase in life span,

while IM did not. When IM was combined with troxacitabine at 10 and 25 mg/kg in the KBM5 xenograft model, a further increase in life span was observed and some mice achieved long-term survival. These data indicate that the combination of troxacitabine and IM has significant preclin. activity in advanced CML and that clin. evaluation of this combination is warranted.

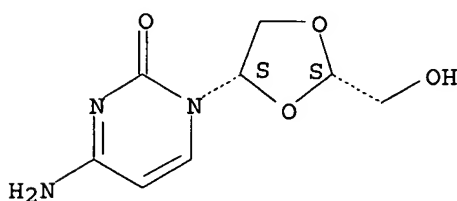
IT 145918-75-8, Troxatyl

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-6 (Pharmacology)

ST troxacitabine **imatinib mesylate** antitumor resistance chronic myeloid leukemia

IT Drug resistance

(antitumor; troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

IT Leukemia

(chronic myelocytic; troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

IT Antitumor agents

(resistance to; troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

IT Antitumor agents

Human

(troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

IT 145918-75-8, Troxatyl 220127-57-1, Gleevec

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (troxacitabine and **imatinib mesylate** combination therapy of chronic myeloid leukemia)

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 6 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2004:868814 HCAPLUS

DOCUMENT NUMBER: 142:168637

TITLE: Nucleoside analogs and antimetabolite therapies for myelodysplastic syndrome

AUTHOR(S): Foss, Francine M.

CORPORATE SOURCE: Department of Hematology-Oncology and Experimental Therapeutics, Bone Marrow Transplant Program, Tufts New England Medical Center, Boston, MA, 02111, USA

SOURCE: Best Practice & Research, Clinical Haematology (2004),

17(4), 573-584
CODEN: BPRCA5
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

ED Entered STN: 20 Oct 2004

AB A review. Myelodysplastic syndrome (MDS) is a heterogeneous group of clonal hematopoietic disorders. Therapeutic interventions for MDS other than allogeneic bone marrow transplantation have been palliative. Because most of the patients are elderly and may not be candidates for ablative transplant conditioning regimens, treatment has focused on supportive care. Recently, several novel biol. and chemotherapeutic agents have demonstrated activity in MDS and are being incorporated into the treatment paradigm. These agents are based on specific mechanisms aimed at angiogenesis in the bone marrow, secretion of growth factors and/or their receptors, and modulators in their intracellular pathways. Several agents are in the initial stages of clin. trial, including anti-vascular endothelial growth factor, bevacizumab, receptor **tyrosine kinase inhibitors**, farnesyl transferase **inhibitors**, protein kinase C inhibitors, matrix metalloproteinase inhibitors and other agents such as thalidomide and arsenic trioxide. Novel chemotherapeutic agents include topoisomerase inhibitors such as topotecan and rubitecan, and deoxyadenosine analogs such as troxacitabine, tezacitabine, and clofarabine. Prognostic factors predicting response in MDS patients treated with intensive chemotherapy have been identified and include younger age and favorable cytogenetics.

IT 145918-75-8, Troxacitabine

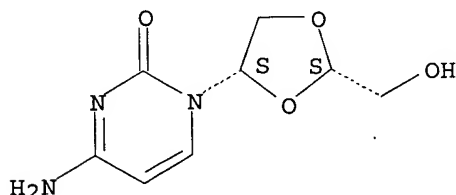
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(deoxyadenosine analogs such as troxacitabine for patients with myelodysplastic syndrome are discussed)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-0 (Pharmacology)

IT 145918-75-8, Troxacitabine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(deoxyadenosine analogs such as troxacitabine for patients with myelodysplastic syndrome are discussed)

IT 340830-03-7

RL: BSU (Biological study, unclassified); BIOL (Biological study) (receptor **tyrosine kinase inhibitor** is in

initial stages of clin. trial for myelodysplastic syndrome in human)

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

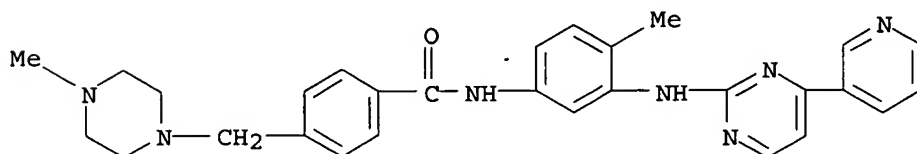
L89 ANSWER 7 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 2004:599447 HCAPLUS
DOCUMENT NUMBER: 142:85532
TITLE: Biology of chronic myeloid leukemia and possible therapeutic approaches to imatinib-resistant disease
AUTHOR(S): Yoshida, Chikashi; Melo, Junia V.
CORPORATE SOURCE: Department of Haematology, Hammersmith Hospital, Imperial College London, London, UK
SOURCE: International Journal of Hematology (2004), 79(5), 420-433
CODEN: IJHEEY; ISSN: 0925-5710
PUBLISHER: Carden Jennings Publishing
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 27 Jul 2004
AB A review. Chronic myeloid leukemia (CML) is a stem cell disorder caused by a constitutively activated **tyrosine kinase**, the Bcr-Abl oncoprotein. An **inhibitor** of this **tyrosine kinase**, **imatinib mesylate**, is rapidly becoming the first-line therapy for CML. However, the development of resistance to this drug is a frequent setback, particularly in patients in advanced phases of the disease. Several mechanisms of resistance have been described, the most frequent of which are amplification and/or mutations of the BCR-ABL gene. To overcome resistance, several approaches have been studied in vitro and in vivo. They include dose escalation of imatinib, combination of imatinib with chemotherapeutic drugs, alternative Bcr-Abl inhibitors, inhibitors of kinases downstream of Bcr-Abl, farnesyl and geranylgeranyl transferase inhibitors, histone deacetylase, proteasome and cyclin-dependent kinase inhibitors, arsenic trioxide, hypomethylating agents, troxacitabine, targeting Bcr-Abl mRNA, and immunomodulatory strategies. It is important to understand that these approaches differ in efficiency, which is often dependent on the mechanisms of resistance. Further investigations into the mol. mechanisms of disease and how to specifically target the abnormal processes will guide the design of new treatment modalities in future clin. trials.
IT 220127-57-1, **Imatinib mesylate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dose escalation, combination with chemotherapeutic drugs, alternative Bcr-Abl, kinase, transferase inhibitors and targeting Bcr-Abl mRNA and immunomodulatory strategies are possible therapeutic approaches to imatinib-resistant CML)
RN 220127-57-1 HCAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]aminol]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5

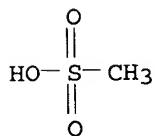
CMF C29 H31 N7 O



CM 2

CRN 75-75-2

CMF C H4 O3 S



CC 1-0 (Pharmacology)

IT 220127-57-1, Imatinib mesylate

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)(dose escalation, combination with chemotherapeutic drugs, alternative
Bcr-Abl, kinase, transferase inhibitors and targeting Bcr-Abl mRNA and
immunomodulatory strategies are possible therapeutic approaches to
imatinib-resistant CML)

IT 145918-75-8, Troxacitabine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)(troxacitabine is one of possible therapeutic approach to
imatinib-resistant chronic myeloid leukemia disease both in vitro and
in vivo)REFERENCE COUNT: 164 THERE ARE 164 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L89 ANSWER 8 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 2003:737931 HCAPLUS

DOCUMENT NUMBER: 139:255332

TITLE: Method for selecting antitumor drug
sensitivity-determining factors and method for
predicting antitumor drug sensitivity using the
selected factorsINVENTOR(S): Aoki, Yuko; Hasegawa, Kiyoshi; Ishii, Nobuya; Mori,
Kazushige

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076660	A1	20030918	WO 2002-JP2354	20020313
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,			

GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
 GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2478640	AA	20030918	CA 2002-2478640	20020313
EP 1483401	A1	20041208	EP 2002-705127	20020313

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: WO 2002-JP2354 W 20020313

ED Entered STN: 19 Sep 2003

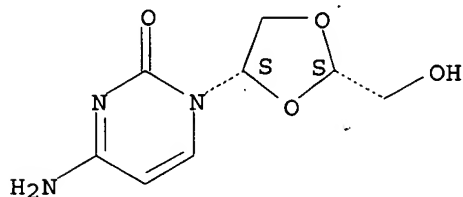
AB Based on drug sensitivity data and extensive gene expression data, a model was constructed by multivariate anal. with the partial least squares method type 1. Further, the model was optimized using modeling power and genetic algorithm. Thereby, the degree of contribution of the resp. genes to drug sensitivity was determined to select genes with a high degree of contribution. In addition, the levels of gene expression in specimens were analyzed, and then the drug sensitivity was predicted based on the model. The predicted values agreed well with those drug sensitivity values determined exptl. The drug sensitivity-predicting method provided by the present invention enables assessment of the effectiveness of a drug prior to administration using small quantities of specimens associated with diseases such as cancer. Since this enables the selection of the most suitable drug for each patient, the present invention is very useful in improving a patient's quality of life (QOL).

IT 145918-75-8, Troxacitabine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (method for selecting antitumor drug sensitivity-determining factors and predicting antitumor drug sensitivity using the selected factors)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IC ICM C12Q001-68
 ICS G06K009-62; G06F017-17

CC 1-6 (Pharmacology)
 Section cross-reference(s): 2

IT 51-21-8, 5-FU 66-22-8, 2,4(1H,3H)-Pyrimidinedione, biological studies
 147-94-4, Ara-C 2207-75-2, Potassium oxonate 2353-33-5, Decitabine
 3094-09-5, Furtulon 4291-63-8, Cladribine 7689-03-4, Camptothecin
 10540-29-1, Tamoxifen 15663-27-1, Cisplatin 17902-23-7, Tegafur
 20830-81-3, Daunomycin 25316-40-9, Adriamycin 33069-62-4, Taxol
 41575-94-4, Carboplatin 53714-56-0, Leuporelin 56420-45-2, Epirubicin
 58957-92-9, Idarubicin 61422-45-5, Carmofur 75607-67-9 82640-04-8,
 LY156758 90357-06-5, ZD 176334 91421-42-0, 9-Nitrocamptothecin
 91421-43-1, 9-Aminocamptothecin 100286-90-6, CPT-11 103766-25-2,
 5-Chloro-2,4-dihydroxypyridine 105149-00-6, TZP4238 107868-30-4,
 FCE24304 110417-88-4, Dolastatin 10 112809-51-5, CGS 20267
 114977-28-5, Taxotere 115767-74-3, TAT59 119804-96-5, DMDC
 120511-73-1, ZD 1033 120685-11-2, CGP41251 123884-00-4, Dolastatin 15
 123948-87-8, Topotecan 126723-15-7, Dolastatin 14 145918-75-8,

Troxacitabine 149606-27-9, T2T 1027 154361-50-9, Xeloda 159776-69-9,
 Cemadotin 160237-25-2, BMS 184476 169869-90-3, DX-8951f 171179-06-9,
 PD 158780 172481-83-3, BMS 188797 172903-00-3, BBR 3464 182133-25-1,
 LY353381 182167-03-9, EM800 183319-69-9, CP 358774 184475-35-2, ZD
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 247550 220127-57-1, STI-571 220997-97-7,
 BN-80915 252916-29-3, SU6668 253863-00-2, L778123 284461-73-0, BAY
 439006 437755-78-7, GW 2016 443913-73-3, ZD6474 601517-74-2, GW 2286
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(method for selecting antitumor drug sensitivity-determining factors and
 predicting antitumor drug sensitivity using the selected factors)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 9 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 2003:202456 HCAPLUS

DOCUMENT NUMBER: 138:231710

TITLE: Treatment of chronic myelogenous leukemia, resistant
 or intolerant to STI571, involving homoharringtonine
 alone or combined with other agents

INVENTOR(S): Robin, Jean-Pierre; Mahon, Francois-Xavier;
 Maisonneuve, Herve; Maloisel, Frederick; Blanchard,
 Julie

PATENT ASSIGNEE(S): Oncopharm Corporation, USA

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020252	A2	20030313	WO 2002-IB3992	20020905
WO 2003020252	A3	20030619		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1443933	A2	20040811	EP 2002-772653	20020905
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
US 2004019036	A1	20040129	US 2003-397267	20030327
PRIORITY APPLN. INFO.:			US 2001-316967P	P 20010905
			WO 2002-IB3992	W 20020905

ED Entered STN: 14 Mar 2003

AB The present invention concerns a method of treating chronic myelogenous leukemia (CML), a related myeloproliferative disorder or a Ph-pos. acute lymphocytic leukemia in a subject animal, comprising: (a) selecting or identifying an animal suffering from chronic myelogenous leukemia or a related myeloproliferative disorder and showing resistance or intolerance

to treatment with STI571; and (b) administering to the animal homoharringtonine. In a preferred embodiment, the animal is a human being. Significant sensitivity to homoharringtonine was observed in progenitors from patients relapsing on STI571 therapy both before and after relapse,, strongly implying that in CML blast crisis cells refractory to STI751 there is no significant cross-resistance to homoharringtonine.

IT 220127-57-1, STI571

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic myelogenous leukemia, resistant or intolerant to STI571, treatment with homoharringtonine alone or combined with other agents)

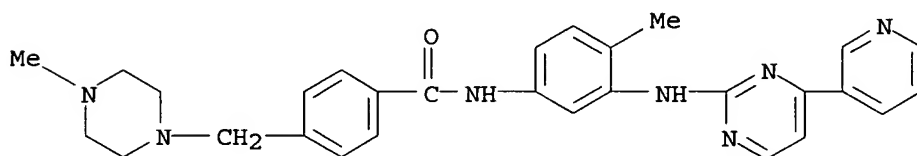
RN 220127-57-1 HCAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]aminophenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5

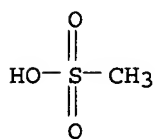
CMF C29 H31 N7 O



CM 2

CRN 75-75-2

CMF C H4 O3 S



IC ICM A61K031-00

CC 1-6 (Pharmacology)

IT 26833-87-4, Homoharringtonine 220127-57-1, STI571

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic myelogenous leukemia, resistant or intolerant to STI571, treatment with homoharringtonine alone or combined with other agents)

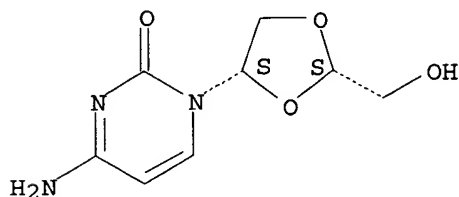
IT 147-94-4, Cytarabine 2353-33-5, Decitabine 25322-68-3D, Peg, conjugates with interferons 145918-75-8, Troxacitabine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic myelogenous leukemia, resistant or intolerant to STI571, treatment with homoharringtonine alone or combined with other agents)

L89 ANSWER 10 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 12
ACCESSION NUMBER: 2003:621850 HCAPLUS

DOCUMENT NUMBER: 140:228562
 TITLE: Phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase
 AUTHOR(S): Giles, Francis J.; Feldman, Eric J.; Roboz, Gail J.; Larson, Richard A.; Mamus, Steven W.; Cortes, Jorge E.; Verstovsek, Srdan; Faderl, Stefan; Talpaz, Moshe; Beran, Miloslav; Albitar, Maher; O'Brien, Susan M.; Kantarjian, Hagop M.
 CORPORATE SOURCE: M.D. Anderson Cancer Center, Department of Leukemia, University of Texas, Houston, TX, 77030, USA
 SOURCE: Leukemia Research (2003), 27(12), 1091-1096
 CODEN: LEREDD; ISSN: 0145-2126
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 13 Aug 2003
 AB A phase II study of troxacitabine, a non-natural dioxolane nucleoside L-enantiomer, was conducted in patients with chronic myelogenous leukemia in blastic phase (CML-BP). Patients were untreated for BP, or treated with **imatinib mesylate** (IM) as sole prior therapy for BP. Troxacitabine was given as an i.v. infusion over 30 min daily for 5 days at a dose of 8.0 mg/m² per day. Thirty-one patients, 29 (93%) of whom had failed prior IM therapy, received 51 courses of therapy. Grade 3 or 4 toxicities included stomatitis (4%), hand-foot syndrome (18%), and skin rash (12%). Four patients (13%) responded. Troxacitabine-based combinations merit study in IM-resistant CML.
 IT 145918-75-8, Troxacitabine
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)
 RN 145918-75-8 HCAPLUS
 CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



CC 1-6 (Pharmacology)
 ST antitumor troxacitabine **imatinib mesylate** resistant chronic myelogenous leukemia; dioxolane nucleoside analog antitumor **imatinib mesylate** resistant myelogenous leukemia
 IT Drug resistance
 (antitumor; phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)
 IT Leukemia
 (chronic myelocytic; phase II study of troxacitabine, a novel dioxolane

nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

IT Antitumor agents

(chronic myelogenous leukemia; phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

IT Human

(phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

IT Antitumor agents

(resistance to; phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

IT 145918-75-8, Troxacitabine

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

IT 220127-57-1, **Imatinib mesylate**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(resistance; phase II study of troxacitabine, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib mesylate**-resistant chronic myelogenous leukemia in blastic phase)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 11 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:80347 HCAPLUS

DOCUMENT NUMBER: 140:122775

TITLE: Treatment of chronic myelogenous leukemia, resistant or intolerant to STI571, involving homoharringtonine alone or combined with other agents

INVENTOR(S): Robin, Jean-pierre; Mahon, Francois-xavier; Maisonneuve, Herve; Maloisel, Frederick; Blanchard, Julie

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of Appl. No. PCT/IB02/03992.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004019036	A1	20040129	US 2003-397267	20030327
WO 2003020252	A2	20030313	WO 2002-IB3992	20020905
WO 2003020252	A3	20030619		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-316967P P 20010905
 WO 2002-IB3992 A2 20020905

ED Entered STN: 01 Feb 2004

AB The invention concerns a method of treating chronic myelogenous leukemia, a related myeloproliferative disorder or a Ph-pos. acute lymphocytic leukemia in a subject animal, comprising: (a) selecting or identifying an animal suffering from chronic myelogenous leukemia or a related myeloproliferative disorder and showing resistance or intolerance to treatment with STI571; and (b) administering to the animal homoharringtonine. In a preferred embodiment, the animal is a human.

IT 220127-57-1, STI571

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of CML, resistant or intolerant to STI571, involving homoharringtonine alone or combined with other agents).

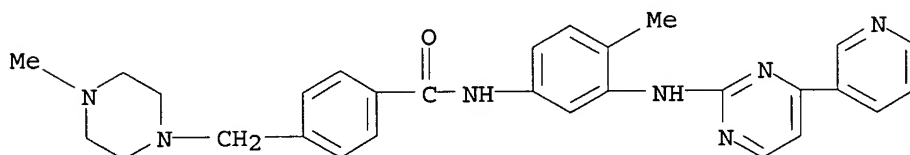
RN 220127-57-1 HCAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5

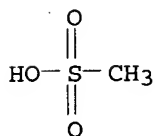
CMF C29 H31 N7 O



CM 2

CRN 75-75-2

CMF C H4 O3 S



IC ICM A61K031-55

NCL 514214030

CC 1-6 (Pharmacology)

Section cross-reference(s): 15, 63

IT 147-94-4, Cytarabine 26833-87-4, Homoharringtonine 220127-57-1, STI571

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of CML, resistant or intolerant to STI571, involving homoharringtonine alone or combined with other agents)

IT 2353-33-5, Decitabine 145918-75-8, Troxacitabine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of CML, resistant or intolerant to STI571, involving homoharringtonine alone or combined with other agents)

L89 ANSWER 12 OF 54 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:356264 HCAPLUS

DOCUMENT NUMBER: 138:348696

TITLE: Pharmaceutical compositions for the treatment of leukemia comprising dioxolane nucleosides analogs

INVENTOR(S): Jolivet, Jacques; Giles, Francis J.; Kantarjian, Hagop

PATENT ASSIGNEE(S): Shire Biochem Inc., Can.

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037344	A1	20030508	WO 2002-CA1687	20021104
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003125305	A1	20030703	US 2002-286960	20021104
US 6645972	B2	20031111		
EP 1441733	A1	20040804	EP 2002-771956	20021104
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
PRIORITY APPLN. INFO.:			US 2001-330891P	P 20011102
			WO 2002-CA1687	W 20021104

OTHER SOURCE(S): MARPAT 138:348696

ED Entered STN: 09 May 2003

AB The present invention provides a novel method for treating leukemia in a host that has been previously treated with a Bcr-Abl **tyrosine kinase inhibitor** comprising administering to the host a therapeutically effective amount of a dioxolane nucleoside analog.

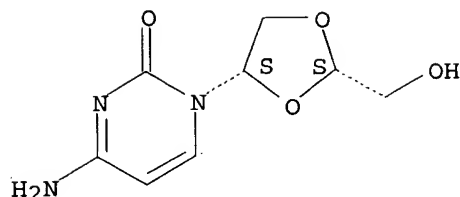
IT 145918-75-8, Troxatyl

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (dioxolane nucleoside analog for treatment of leukemia)

RN 145918-75-8 HCAPLUS

CN 2(1H)-Pyrimidinone, 4-amino-1-[(2S,4S)-2-(hydroxymethyl)-1,3-dioxolan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IC ICM A61K031-506
 ICS A61P035-02
 CC 1-6 (Pharmacology)
 IT 138238-67-2, Bcr-Abl **tyrosine kinase**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (dioxolane nucleoside analog for treatment of leukemia)
 IT 145918-75-8, Troxatyl 220127-57-1, **Imatinib**
mesylate
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (dioxolane nucleoside analog for treatment of leukemia)
 REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' -
 CONTINUE? (Y)/N:y

L89 ANSWER 13 OF 54 MEDLINE on STN DUPLICATE 7
 ACCESSION NUMBER: 2004043980 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14745859
 TITLE: New agents in acute myeloid leukemia and other myeloid disorders.
 AUTHOR: Ravandi Farhad; Kantarjian Hagop; Giles Francis; Cortes Jorge
 CORPORATE SOURCE: Department of Leukemia, The University of Texas M D Anderson Cancer Center, Houston, Texas 77030, USA.. fravandi@mdanderson.org
 SOURCE: Cancer, (2004 Feb 1) 100 (3) 441-54. Ref: 140
 Journal code: 0374236. ISSN: 0008-543X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 200402
 ENTRY DATE: Entered STN: 20040128
 Last Updated on STN: 20040220
 Entered Medline: 20040219
 ED Entered STN: 20040128
 Last Updated on STN: 20040220
 Entered Medline: 20040219
 AB Over the past several decades, improvements in chemotherapeutic agents and supportive care have resulted in significant progress in treating patients with acute myeloid leukemia (AML). More recently, advances in understanding the biology of AML have resulted in the identification of new therapeutic targets. The success of all-trans-retinoic acid in acute

promyelocytic leukemia and of imatinib mesylate in chronic myeloid leukemia have demonstrated that targeted therapy may be more effective and less toxic when well defined targets are available. At the same time, understanding mechanisms of drug resistance and means to overcome them has led to modification of some of the existing cytotoxic agents. Rational design and conduct of clinical trials is necessary to ensure that the full potential of these new agents is realized.

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CT Check Tags: Comparative Study; Female; Male

*Antineoplastic Agents: TU, therapeutic use

Cyclosporine: TU, therapeutic use

*Cytosine: AA, analogs & derivatives

Cytosine: TU, therapeutic use

*Deoxycytidine: AA, analogs & derivatives

Deoxycytidine: TU, therapeutic use

Dioxolanes: TU, therapeutic use

Humans

*Immunosuppressive Agents: TU, therapeutic use

Immunotherapy: MT, methods

Leukemia, Myelocytic, Acute: DI, diagnosis

*Leukemia, Myelocytic, Acute: DT, drug therapy

Leukemia, Myelocytic, Acute: MO, mortality

Prognosis

Randomized Controlled Trials

Risk Assessment

Severity of Illness Index

Survival Analysis

Treatment Outcome

RN 103882-84-4 (gemcitabine); 145918-75-8 (troxacitabine);

59865-13-3 (Cyclosporine); 71-30-7 (Cytosine); 951-77-9 (Deoxycytidine)

CN 0 (Antineoplastic Agents); 0 (Dioxolanes); 0 (Immunosuppressive Agents)

=> d ibib ed ab hitind 14-45

YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' -
CONTINUE? (Y)/N:y

L89 ANSWER 14 OF 54 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2004098430 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14988742
TITLE: Gateways to clinical trials.
AUTHOR: Bayes M; Rabasseda X; Prous J R
CORPORATE SOURCE: Prous Science, PO Box 540, 08080 Barcelona, Spain..
mbayes@prous.com
SOURCE: Methods and findings in experimental and clinical
pharmacology, (2004 Jan-Feb) 26 (1) 53-84. Ref: 200
Journal code: 7909595. ISSN: 0379-0355.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040302
Last Updated on STN: 20040510
Entered Medline: 20040507
ED Entered STN: 20040302
Last Updated on STN: 20040510

Entered Medline: 20040507

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies Knowledge Area of Prous Science Integrity, the drug discovery and development portal, <http://integrity.prous.com>. This issue focuses on the following selection of drugs: Abetimus sodium, Ad5-FGF4, adeno-Interferon gamma, AE-941, AERx, alemtuzumab, alicaforsen sodium, almotriptan, alparadin, anakinra, anatumomab mafenatox, ANG-453, anti-CTLA-4 Mab, AP-12009, aprepitant, aripiprazole, arsenic trioxide, astemizole, atlizumab, atomoxetine hydrochloride; Bevacizumab, BG-9928, BMS-188667, botulinum toxin type B, BufferGel; Caffeine, CDP-870, cetuximab, cilomilast, ciluprevir, clofarabine, continuous erythropoiesis receptor activator, CP-461; Darbepoetin alfa, deferasirox, desloratadine, desoxyepothilone B, diflomotecan, dolasetron, drotrecogin alfa (activated), duloxetine hydrochloride; ED-71, efalizumab, efaproxiral sodium, EKB-569, eletriptan, EMD-72000, enfuvirtide, erlotinib hydrochloride, escitalopram oxalate, etoricoxib; Fampridine, ferumoxytol, fondaparinux sodium; Gadofosveset sodium, gastrazole, gefitinib, gemtuzumab ozogamicin, gepirone hydrochloride glutamine; hLM609, HSPPC-96, human insulin; IDD-1, **imatinib mesylate**, indisulam, inhaled insulin, ixabepilone; Keratinocyte growth factor; Lapatinib, laquinimod, LDP-02, LE-SN38, levetiracetam, levosimendan, licofelone, liposomal doxorubicin, liposomal NDDP, lopinavir, lumiracoxib, LY-156735; Morphine hydrochloride, morphine-6-glucuronide, motexafin gadolinium, MS-27-275, MVA-5T4, MVA-Muc1-IL-2; Nemifitide ditriflutate, neridronic acid nitronaproxen, NSC-683864, NSC-703940, NVP-LAF-237; Oblimersen sodium, ocinaplon, oncomyc-NG, OPC-28326, ortataxel, ospemifene; Palonosetron hydrochloride, PEG-filgrastim peginterferon alfa-2(a), peginterferon alfa-2b, pegsunercept, pemetrexed disodium, pregabalin, prilocaine, pyridoxamine; RDP-58, recombinant glucagon-like peptide-1 (7-36) amide, recombinant human ApoA-I milano/phospholipid complex; SB-715992, soblidotin, sodium dichloroacetate, St. John's Wort extract; TAS-102, terfenadine, TG-1024, TG-5001, 4'-Thio-ara-C, tipranavir, topixantrone hydrochloride, trabectedin, transdermal selegiline, trimethoprim, **troxacitabine**, TT-232; Vatalanib succinate, vinflunine; Ximelagatran; Ziprasidone hydrochloride, Zoledronic acid monohydrate.

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CT *Clinical Trials: SN, statistics & numerical data
 *Databases, Factual: SN, statistics & numerical data
 Humans
 Statistics

L89 ANSWER 15 OF 54 MEDLINE on STN DUPLICATE 13
 ACCESSION NUMBER: 2004035206 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14735233
 TITLE: Gateways to clinical trials.
 AUTHOR: Bayes M; Rabasseda X; Prous J R
 CORPORATE SOURCE: Prous Science, Barcelona, Spain.. mbayes@prous.com
 SOURCE: Methods and findings in experimental and clinical pharmacology, (2003 Dec) 25 (10) 831-55.
 Journal code: 7909595. ISSN: 0379-0355.
 PUB. COUNTRY: Spain
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200404
 ENTRY DATE: Entered STN: 20040122
 Last Updated on STN: 20040501
 Entered Medline: 20040430

ED Entered STN: 20040122
 Last Updated on STN: 20040501
 Entered Medline: 20040430

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies Knowledge Area of Prous Science Integrity, the drug discovery and development portal, <http://integrity.prous.com>. This issue focuses on the following selection of drugs: Abetimus sodium, adalimumab, alefacept, alemtuzumab, almotriptan, AMGN-0007, anakinra, anti-CTLA-4 Mab, L-arginine hydrochloride, arzoxifene hydrochloride, astemizole, atazanavir sulfate, atlizumab; Belimumab, BG-9928, binodenoson, bosentan, botulinum toxin type B, bovine lactoferrin, BufferGel; Caspofungin acetate, ciclesonide, cilomilast, ciluprevir, clofarabine, CVT-3146; Darbepoetin alfa, desloratadine, diflomotecan, doripenem, dronedarone hydrochloride, drotrecogin alfa (activated), DT388-GM-CSF, duloxetine hydrochloride, E-5564, efalizumab, enfuvirtide, esomeprazole magnesium, estradiol acetate, ETC-642, exenatide, exisulind, ezetimib; Febuxostat; Gallium maltolate, ganirelix acetate, garenoxacin mesilate, gefitinib; H11, HuMax; IL-15, IDD-1, IGIV-C, **imatinib mesylate**, ISIS-14803, ITF-1697, ivabradine hydrochloride; KRN-5500; L-365260, levetiracetam, levosimendan, licofelone, linezolid, LJP-1082, lopinavir lumiracoxib; MCC-478, melatonin, morphine hydrochloride, morphine-6-glucuronide, moxidectin; N-Acetylcarnosine, natalizumab, NM-702, NNC-05-1869, NSC-703940; Ocinaclone OM-89, omalizumab, omeprazole/ sodium bicarbonate, OPC-28326, ospemifene; PEG-filgrastim peginterferon alfa-2a, pegsunercept, pirfenidone, pralmorelin, pregabalin; Recombinant glucagon-like peptide-1 (7-36) amide, repifermin, RSD-1235; S-8184, selodenoson, sodium dichloroacetate, suberanilohydroxamic acid; TAS-102, terfenadine, teriparatide, tipranavir **troxacitabine**; Ximelagatran; YM-337.

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CT *Clinical Trials
 *Drug Therapy
 Humans

L89 ANSWER 16 OF 54 MEDLINE on STN DUPLICATE 14

ACCESSION NUMBER: 2003053879 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12563614

TITLE: Advanced-phase chronic myeloid leukemia.

AUTHOR: Cortes Jorge; Kantarjian Hagop

CORPORATE SOURCE: Department of Leukemia, The University of Texas, M.D. Anderson Cancer Center, Houston, TX 77030, USA.

SOURCE: Seminars in hematology, (2003 Jan) 40 (1) 79-86. Ref: 70
 Journal code: 0404514. ISSN: 0037-1963.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200310

ENTRY DATE: Entered STN: 20030204
 Last Updated on STN: 20031009
 Entered Medline: 20031008

ED Entered STN: 20030204
 Last Updated on STN: 20031009
 Entered Medline: 20031008

AB Chronic myeloid leukemia (CML) typically runs a biphasic or triphasic course, with diagnoses usually made in the chronic phase (CP). Without effective treatment, patients eventually progress to a blastic phase (BP),

frequently through an intermediate or accelerated phase (AP). Because the definition of AP varies among studies, comparisons of outcome and prognosis are difficult. The management of patients in these advanced phases of the disease has been much less satisfactory than that of patients in CP. Treatment with interferon-alfa (IFNalpha)-based therapy is ineffective for most patients in AP and for all of those in BP.

Imatinib mesylate has demonstrated significant activity AP and BP disease, although the results are inferior compared to treatment in CP. In AP, 82% of patients achieve a hematologic response, with 24% achieving a major cytogenetic remission (MCR). Early MCR (within 3 months of diagnosis) provides a survival advantage over patients who do not achieve this response or achieve it later. In BP, 21% of previously treated patients and 36% of previously untreated patients have responded to imatinib, and up to 17% of patients may achieve a major cytogenetic response. However, responses are frequently short-lived. Several agents are being investigated for treatment of advanced-phase CML, including decitabine (DAC), homoharringtonine (HHT), **troxacitabine**, clofarabine, farnesyl transferase (FTase) inhibitors (FTI), and others. Many have also proven to be synergistic with imatinib in vitro and combination studies are ongoing. Continued investigation of these approaches is needed to improve the long-term prognosis of advanced-phase CML.

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CT Antineoplastic Agents: TU, therapeutic use
 Blast Crisis: PA, pathology
 Humans
 *Leukemia, Myeloid, Chronic: CL, classification
 Leukemia, Myeloid, Chronic: PA, pathology
 *Leukemia, Myeloid, Chronic: TH, therapy
 Prognosis

CN 0 (Antineoplastic Agents)

L89 ANSWER 17 OF 54 MEDLINE on STN

ACCESSION NUMBER: 2002345081 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12087878

TITLE: Gateways to Clinical Trials.

AUTHOR: Bayes M; Rabasseda X; Prous J R

SOURCE: Methods and findings in experimental and clinical pharmacology, (2002 Apr) 24 (3) 159-84. Ref: 150
 Journal code: 7909595. ISSN: 0379-0355.

PUB. COUNTRY: Spain

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200301

ENTRY DATE: Entered STN: 20020629
 Last Updated on STN: 20030111
 Entered Medline: 20030110

ED Entered STN: 20020629
 Last Updated on STN: 20030111
 Entered Medline: 20030110

AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies knowledge area of Prous Science Integrity, the world's first drug discovery and development portal, and provides information on study design, treatments, conclusions and references. This issue focuses on the following selection of drugs: Abiciximab, acetylcholine chloride, acetylcysteine, alefacept, alemtuzumab, alicaforsen, alteplase, aminopterin, amoxicillin sodium,

amphotericin B, anastrozole, argatroban monohydrate, arsenic trioxide, aspirin, atazanavir, atorvastatin, augmerosen, azathioprine; Benzylpenicillin, BMS-284756, botulinum toxin type A, botulinum toxin type B, BQ-123, budesonide, BXT-51072; Calcium folinate, carbamazepine, carboplatin, carmustine, ceftriaxone sodium, cefuroxime axetil, chorionic gonadotropin (human), cimetidine, ciprofloxacin hydrochloride, cisplatin, citalopram hydrobromide, cladribine, clarithromycin, clavulanic acid, clofarabine, clopidogrel hydrogensulfate, clotrimazole, CNI-1493, colesevelam hydrochloride, cyclophosphamide, cytarabine; Dalteparin sodium, daptomycin, darbepoetin alfa, debrisoquine sulfate, dexrazoxane, diaziquone, didanosine, docetaxel, donepezil, doxorubicin hydrochloride liposome injection, DX-9065a; Eberconazole, ecogramostim, eletriptan, enoxaparin sodium, epoetin, epoprostenol sodium, erlizumab, ertapenem sodium, ezetimibe; Fampridine, fenofibrate, filgrastim, fluconazole, fludarabine phosphate, fluorouracil, 5-fluorouracil/epinephrine, fondaparinux sodium, formoterol fumarate; Gabapentin, gemcitabine, gemfibrozil, glatiramer; Heparin sodium, homoharringtonine; Ibuprofen, iloprost, **imatinib mesilate**, imiquimod, interferon alpha-2b, interferon alpha-2c, interferon-beta; KW-6002; Lamotrigine, lanoteplase, metoprolol tartrate, mitoxantrone hydrochloride; Naproxen sodium, naratriptan, Natalizumab, nelfinavir mesilate, nevirapine, nifedipine, NSC-683864; Oral heparin; Paclitaxel, peginterferon alfa-2b, phenytoin, pimecrolimus, piperacillin, pleconaril, pramipexole hydrochloride, prednisone, pregabalin, progesterone; Rasburicase, ravuconazole, reteplase, ribavirin, rituximab, rizatriptan, rosiglitazone maleate, rotigotine; Semaxanib, sildenafil citrate, simvastatin, stavudine, sumatriptan; Tacrolimus, tamoxifen citrate, tanomastat, tazobactam, telithromycin, tenecteplase, tolafentrine, tolterodine tartrate, triamcinolone acetonide, trimetazidine, **troxacitabine**; Valproic acid, vancomycin hydrochloride, vincristine, voriconazole, Warfarin sodium; Ximelagatran, Zidovudine, zolmitriptan.

CT *Clinical Trials

*Drug Therapy
Humans

L89 ANSWER 18 OF 54 MEDLINE on STN
 ACCESSION NUMBER: 2002687859 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12446421
 TITLE: Chronic myelogenous leukemia.
 AUTHOR: Druker Brian J; O'Brien Stephen G; Cortes Jorge; Radich Jerald
 CORPORATE SOURCE: University of Newcastle, Royal Victoria Infirmary, Newcastle Upon Tyne, United Kingdom.
 SOURCE: Hematology / the Education Program of the American Society of Hematology. American Society of Hematology. Education Program, (2002) 111-35. Ref: 173
 Journal code: 100890099. ISSN: 1520-4391.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200308
 ENTRY DATE: Entered STN: 20021214
 Last Updated on STN: 20030828
 Entered Medline: 20030827
 ED Entered STN: 20021214
 Last Updated on STN: 20030828
 Entered Medline: 20030827

AB The treatment options for chronic myelogenous leukemia (CML) continue to evolve rapidly. **Imatinib mesylate** (Gleevec, **Glivec**, formerly STI571) has continued to show remarkable clinical benefits and the updated results with this agent are reviewed. As relapses using single agent imatinib have occurred, particularly in advanced phase patients, the issue of whether combinations of other antileukemic agents with imatinib may yield improved results is addressed. In addition, data on new agents that have potential in the treatment of CML are reviewed. These agents are presented in the context of their molecular mechanism of action. The most recent data for stem cell transplantation, along with advances in nonmyeloablative transplants, are also reviewed. In Section I, Drs. Stephen O'Brien and Brian Druker update the current status of clinical trials with imatinib and review ongoing investigations into mechanisms of resistance and combinations of imatinib with other agents. They also present their views on integration of imatinib with other therapies. In Section II, Dr. Jorge Cortes describes the most recent data on novel therapies for CML, including farnesyl transferase inhibitors, arsenic trioxide, decitabine, and **troxatyl**, among others. These agents are discussed in the context of their molecular mechanism of action and rationale for use. In Section III, Dr. Jerald Radich updates the results of stem cell transplants for CML, including emerging data on nonmyeloablative transplants. He also presents data on using microarrays to stratify patients into molecularly defined risk groups.

CT *Antineoplastic Agents: TU, therapeutic use
Clinical Trials
*Hematopoietic Stem Cell Transplantation: MT, methods
Hematopoietic Stem Cell Transplantation: MO, mortality
Humans
Leukemia, Myeloid, Chronic: MO, mortality
*Leukemia, Myeloid, Chronic: TH, therapy
Piperazines: AD, administration & dosage
Piperazines: TU, therapeutic use
Pyrimidines: AD, administration & dosage
Pyrimidines: TU, therapeutic use
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Survival Analysis
RN 152459-95-5 (imatinib)
CN 0 (Antineoplastic Agents); 0 (Piperazines); 0 (Pyrimidines)

L89 ANSWER 19 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 15

ACCESSION NUMBER: 2001380875 EMBASE
TITLE: Chronic myelogenous leukemia.
AUTHOR: Kalidas M.; Kantarjian H.; Talpaz M.
CORPORATE SOURCE: Dr. M. Talpaz, Department of Bioimmunotherapy, M.D.
Anderson Cancer Center, Box 422, 1515 Holcombe Blvd,
Houston, TX 77030, United States.
mtalpaz@mail.mdanderson.org
SOURCE: Journal of the American Medical Association, (22 Aug 2001)
286/8 (895-898).
Refs: 48
ISSN: 0098-7484 CODEN: JAMAAP
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
025 Hematology
037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

CT Medical Descriptors:

*chronic myeloid leukemia: DT, drug therapy
 *chronic myeloid leukemia: ET, etiology
 *chronic myeloid leukemia: TH, therapy
 pathophysiology
 Philadelphia 1 chromosome
 karyotype
 fluorescence in situ hybridization
 reverse transcription polymerase chain reaction
 malignant transformation
 stem cell transplantation
 fever: SI, side effect
 chill: SI, side effect
 fatigue: SI, side effect
 arthralgia: SI, side effect
 anorexia: SI, side effect
 weight reduction
 nausea: SI, side effect
 vomiting: SI, side effect
 fluid retention
 human
 review

priority journal

Drug Descriptors:

*BCR ABL protein: EC, endogenous compound
 *busulfan: AE, adverse drug reaction
 *busulfan: DT, drug therapy
 *hydroxyurea: AE, adverse drug reaction
 *hydroxyurea: CB, drug combination
 *hydroxyurea: DT, drug therapy
 *alpha interferon: AE, adverse drug reaction
 *alpha interferon: CB, drug combination
 *alpha interferon: DT, drug therapy
 *2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: AE, adverse drug reaction
 *2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine: DT, drug therapy
 protein tyrosine kinase: EC, endogenous compound
 messenger RNA: EC, endogenous compound
 homoharringtonine: DT, drug therapy
 5 aza 2' deoxycytidine: DT, drug therapy
 troxacitabine: DT, drug therapy
 cytosine derivative: DT, drug therapy
 vaccine: DT, drug therapy
 cytarabine: AE, adverse drug reaction
 cytarabine: CB, drug combination
 cytarabine: DT, drug therapy
 protein tyrosine kinase inhibitor: AE, adverse drug reaction
 protein tyrosine kinase inhibitor: DT, drug therapy
 unclassified drug

gleevec

RN (busulfan) 55-98-1; (hydroxyurea) 127-07-1; (2 [2 methyl 5 [4 (4 methyl 1 piperazinylmethyl)benzamido]anilino] 4 (3 pyridyl)pyrimidine) 152459-95-5;
 (protein tyrosine kinase) 80449-02-1;
 (homoharringtonine) 26833-87-4; (5 aza 2' deoxycytidine) 2353-33-5;
 (cytarabine) 147-94-4, 69-74-9

CN (1) Sti 571; (2) Gleevec; (3) Cgp 57148

CO (2) Novartis (United States); (3) Novartis (Switzerland)

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on STN

ACCESSION NUMBER: 2004366355 EMBASE
TITLE: Imatinib therapy in chronic myelogenous leukemia:
Strategies to avoid and overcome resistance.
AUTHOR: Hochhaus A.; La Rosee P.
CORPORATE SOURCE: Prof. A. Hochhaus, III Medizinische Klinik, Fakultat
Klinische Medizin Mannheim, Universitat Heidelberg,
Wiesbadener Strasse 7-11, Mannheim 68305, Germany.
hochhaus@uni-hd.de
SOURCE: Leukemia, (2004) 18/8 (1321-1331).
Refs: 109
ISSN: 0887-6924 CODEN: LEUKED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Imatinib is a molecularly targeted therapy that inhibits the oncogenic fusion protein BCR-ABL, the **tyrosine kinase** involved in the pathogenesis of chronic myelogenous leukemia (CML). Selective inhibition of BCR-ABL activity by imatinib has demonstrated efficacy in the treatment of CML, particularly in chronic phase. Some patients, however, primarily those with advanced disease, are either refractory to imatinib or eventually relapse. Relapse with imatinib frequently depends not only on re-emergence of BCR-ABL kinase activity but may also indicate BCR-ABL-independent disease progression not amenable to imatinib inhibition. Results from phase 2/3 trials suggest that rates of resistance and relapse correlate with the stage of disease and with the monitoring parameters - hematologic, cytogenetic and molecular response. These observations and more recent trials with imatinib, combined with insights provided by an increased understanding of the molecular mechanisms of resistance, have established the rationale for strategies to avoid and overcome imatinib resistance in the management of CML patients. To prevent resistance, early diagnosis and prompt treatment with appropriate initial dosing is essential. Management of resistance may include therapeutic strategies such as dose escalation to achieve individual optimal levels, combination therapy, as well as treatment interruption. .COPYRGHT. 2004 Nature Publishing Group All rights reserved.

CT Medical Descriptors:
*chronic myeloid leukemia: DI, diagnosis
*chronic myeloid leukemia: DR, drug resistance
*chronic myeloid leukemia: DT, drug therapy
*chronic myeloid leukemia: ET, etiology
*chronic myeloid leukemia: TH, therapy
drug targeting
protein targeting
drug efficacy
enzyme activity
cancer recurrence
cancer staging
drug response
chromosome analysis
monotherapy
advanced cancer: DI, diagnosis
advanced cancer: DR, drug resistance

advanced cancer: DT, drug therapy
advanced cancer: ET, etiology
minimal residual disease: CO, complication
polymerase chain reaction
gene amplification
gene mutation
cancer survival
amino acid substitution
drug dose regimen
maximum tolerated dose
drug blood level
drug mechanism
low drug dose
allogeneic hematopoietic stem cell transplantation
human
clinical trial
review
nucleotide sequence
priority journal
Drug Descriptors:
*imatinib: CT, clinical trial
*imatinib: CB, drug combination
*imatinib: CR, drug concentration
*imatinib: DO, drug dose
*imatinib: DT, drug therapy
*imatinib: PD, pharmacology
BCR ABL protein: EC, endogenous compound
orosomucoid: EC, endogenous compound
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DO, drug dose
cytarabine: DT, drug therapy
peginterferon: CT, clinical trial
peginterferon: CB, drug combination
peginterferon: DT, drug therapy
alpha2a interferon: CT, clinical trial
alpha2a interferon: CB, drug combination
alpha2a interferon: DT, drug therapy
alpha2b interferon: CT, clinical trial
alpha2b interferon: CB, drug combination
alpha2b interferon: DT, drug therapy
etoposide: CT, clinical trial
etoposide: CB, drug combination
etoposide: CM, drug comparison
etoposide: DT, drug therapy
arsenic trioxide: CT, clinical trial
arsenic trioxide: CB, drug combination
arsenic trioxide: DT, drug therapy
gemtuzumab ozogamicin: CT, clinical trial
gemtuzumab ozogamicin: CB, drug combination
gemtuzumab ozogamicin: DT, drug therapy
mitoxantrone: CT, clinical trial
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
idarubicin: CT, clinical trial
idarubicin: CB, drug combination
idarubicin: DT, drug therapy
cyclophosphamide: CT, clinical trial
cyclophosphamide: CB, drug combination

cyclophosphamide: DT, drug therapy
 vincristine: CT, clinical trial
 vincristine: CM, drug comparison
 vincristine: DT, drug therapy
 doxorubicin: CT, clinical trial
 doxorubicin: CB, drug combination
 doxorubicin: DT, drug therapy
 dexamethasone: CT, clinical trial
 dexamethasone: CB, drug combination
 dexamethasone: DT, drug therapy
 homoharringtonine: CT, clinical trial
 homoharringtonine: CB, drug combination
 homoharringtonine: DT, drug therapy
 tipifarnib: CT, clinical trial
 tipifarnib: CB, drug combination
 tipifarnib: DT, drug therapy
 bortezomib: CT, clinical trial
 bortezomib: CB, drug combination
 bortezomib: DT, drug therapy
 hydroxyurea: CT, clinical trial
 hydroxyurea: CB, drug combination
 hydroxyurea: DT, drug therapy

troxacitabine: CT, clinical trial
 troxacitabine: CB, drug combination
 troxacitabine: DT, drug therapy

lonafarnib: CT, clinical trial
 lonafarnib: CB, drug combination
 lonafarnib: DT, drug therapy

5 aza 2' deoxycytidine: CT, clinical trial
 5 aza 2' deoxycytidine: CB, drug combination
 5 aza 2' deoxycytidine: DT, drug therapy

RN (imatinib) 152459-95-5, **220127-57-1**; (orosomucoid) 79921-18-9;
 (cytarabine) 147-94-4, 69-74-9; (alpha2a interferon) 76543-88-9; (alpha2b
 interferon) 99210-65-8; (etoposide) 33419-42-0; (arsenic trioxide)
 1303-24-8, 1327-53-3, 13464-58-9, 15502-74-6; (mitoxantrone) 65271-80-9,
 70476-82-3; (idarubicin) 57852-57-0, 58957-92-9; (cyclophosphamide)
 50-18-0; (vincristine) 57-22-7; (doxorubicin) 23214-92-8, 25316-40-9;
 (dexamethasone) 50-02-2; (homoharringtonine) 26833-87-4; (tipifarnib)
 192185-72-1; (bortezomib) 179324-69-7, 197730-97-5; (hydroxyurea)
 127-07-1; (**troxacitabine**) **145918-75-8**; (lonafarnib)
 193275-84-2; (5 aza 2' deoxycytidine) 2353-33-5

CN (1) **Gleevec**; (2) **Gleevec**; (3) **Sti 571**

CO (3) Novartis (Switzerland)

GEN GENBANK AAB60394 referred number; GENBANK M14752 referred number

L89 ANSWER 21 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2004228259 EMBASE

TITLE: t(8;21)(q22;q22) in blast phase of chronic myelogenous
 leukemia.

AUTHOR: Yin C.C.; Medeiros L.J.; Glassman A.B.; Lin P.

CORPORATE SOURCE: Dr. P. Lin, Dept. of Hematopathology, Box 72, UT M.D.
 Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX
 77030, United States

SOURCE: American Journal of Clinical Pathology, (2004) 121/6
 (836-842).

Refs: 28

ISSN: 0002-9173 CODEN: AJCPAI

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy
006 Internal Medicine
016 Cancer
025 Hematology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The blast phase of chronic myelogenous leukemia (CML) frequently is associated with cytogenetic evidence of clonal evolution, defined as chromosomal aberrations in addition to the t(9;22)(q34;q11.2). We identified the t(8;21)(q22;q22) and other cytogenetic abnormalities by conventional cytogenetics and fluorescence in situ hybridization in 2 patients with t(9;22)-positive CML at the time of blast phase. The t(8;21), which typically is associated with a distinct subtype of de novo acute myeloid leukemia (AML) carrying the aml1/eto fusion gene, was accompanied by increased bone marrow myeloblasts (33%) in case 1 and extramedullary myeloid sarcoma in case 2, suggesting its possible role in disease progression. In case 1, the leukemic cells in aspirate smears had salmon-colored cytoplasmic granules, and immunophenotypic studies showed that the blasts expressed CD19. These findings suggest that the pathologic features of blast phase CML with the t(8;21) resemble those of de novo AML with the t(8;21).

CT Medical Descriptors:

*chronic myeloid leukemia: DI, diagnosis

*chronic myeloid leukemia: DT, drug therapy

*chronic myeloid leukemia: SU, surgery

*chromosome 22q

*myeloblast

disease association

cytogenetics

cell clone

chromosome aberration

fluorescence in situ hybridization

bone marrow

sarcoma

cancer growth

color

cytoplasm

chromosome 8

chromosome 21

clinical feature

cancer combination chemotherapy

cancer surgery

stem cell transplantation

treatment outcome

human

male

female

case report

human tissue

adult

article

priority journal

Drug Descriptors:

troxacitabine: DT, drug therapy

imatinib: CB, drug combination

imatinib: DT, drug therapy

alpha interferon: CB, drug combination

alpha interferon: DT, drug therapy

cytarabine: CM, drug comparison

cytarabine: DT, drug therapy
 RN (troxacitabine) 145918-75-8; (imatinib) 152459-95-5,
 220127-57-1; (cytarabine) 147-94-4, 69-74-9

L89 ANSWER 22 OF 54 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2004318012 EMBASE
 TITLE: Accelerated and blastic phases of chronic myelogenous leukemia.
 AUTHOR: Giles F.J.; Cortes J.E.; Kantarjian H.M.; O'Brien S.M.
 CORPORATE SOURCE: Dr. F.J. Giles, Department of Leukemia, The University of Texas, M.D. Anderson Cancer Ctr., 1515 H., Houston, TX, United States. fgiles@mdanderson.org
 SOURCE: Hematology/Oncology Clinics of North America, (2004) 18/3 (753-774).
 Refs: 177
 ISSN: 0889-8588 CODEN: HCNAEQ
 PUBLISHER IDENT.: S 0889-8588(04)00010-3
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 016 Cancer
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Although the mechanisms of CML transformation remain poorly understood, recent therapeutic advances moderately have improved the prognosis of patients in AP and BP. Treatment with IFN- α -based regimens are minimally effective for patients in AP and ineffective for those in BP. **Imatinib mesylate** has a significant but generally transient response rate in patients in AP and BP. Hope for progress in this area lies mainly in the development of novel targeted therapies. The more promising agents that are being investigated include decitabine, HHT, **troxacitabine**, clofarabine, farnesyl transferase inhibitors, histone deacetylase inhibitors, and the VEGF and mTOR inhibitors. Many of these approaches may be synergistic with imatinib or the more powerful abl or Src inhibitors that are in development.

CT Medical Descriptors:
 *blast cell crisis
 *chronic myeloid leukemia: DT, drug therapy
 cell cycle
 prognosis
 cancer survival
 drug efficacy
 treatment failure
 diagnostic procedure
 treatment outcome
 basophil
 thrombocyte count
 cytogenetics
 laboratory test
 drug dose regimen
 high risk population
 cancer risk
 risk assessment
 DNA methylation
 Southern blotting
 bone marrow suppression: SI, side effect
 side effect: SI, side effect

mortality
drug cytotoxicity: SI, side effect
stomatitis: SI, side effect
hand foot syndrome: SI, side effect
drug eruption: SI, side effect
human
clinical trial
review
priority journal
Drug Descriptors:
5 aza 2' deoxycytidine: AE, adverse drug reaction
5 aza 2' deoxycytidine: CT, clinical trial
5 aza 2' deoxycytidine: CB, drug combination
5 aza 2' deoxycytidine: DT, drug therapy
troxacitabine: AE, adverse drug reaction
troxacitabine: CT, clinical trial
troxacitabine: CB, drug combination
troxacitabine: DT, drug therapy
protein farnesyltransferase inhibitor: AE, adverse drug reaction
protein farnesyltransferase inhibitor: CT, clinical trial
protein farnesyltransferase inhibitor: CB, drug combination
protein farnesyltransferase inhibitor: DT, drug therapy
histone deacetylase inhibitor: AE, adverse drug reaction
histone deacetylase inhibitor: CT, clinical trial
histone deacetylase inhibitor: CB, drug combination
histone deacetylase inhibitor: DT, drug therapy
vasculotropin inhibitor: AE, adverse drug reaction
vasculotropin inhibitor: CT, clinical trial
vasculotropin inhibitor: CB, drug combination
vasculotropin inhibitor: DT, drug therapy
hydroxyurea: AE, adverse drug reaction
hydroxyurea: CT, clinical trial
hydroxyurea: CB, drug combination
hydroxyurea: DT, drug therapy
daunorubicin: AE, adverse drug reaction
daunorubicin: CT, clinical trial
daunorubicin: CB, drug combination
daunorubicin: DT, drug therapy
cytarabine: AE, adverse drug reaction
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: DT, drug therapy
recombinant alpha interferon: AE, adverse drug reaction
recombinant alpha interferon: CT, clinical trial
recombinant alpha interferon: CB, drug combination
recombinant alpha interferon: DT, drug therapy
peginterferon: AE, adverse drug reaction
peginterferon: CT, clinical trial
peginterferon: CB, drug combination
peginterferon: DT, drug therapy
idarubicin: AE, adverse drug reaction
idarubicin: CT, clinical trial
idarubicin: CB, drug combination
idarubicin: DT, drug therapy
arsenic trioxide: AE, adverse drug reaction
arsenic trioxide: CT, clinical trial
arsenic trioxide: CB, drug combination
arsenic trioxide: DT, drug therapy
lonafarnib: AE, adverse drug reaction
lonafarnib: CT, clinical trial

lonafarnib: CB, drug combination
lonafarnib: DT, drug therapy
tipifarnib: AE, adverse drug reaction
tipifarnib: CT, clinical trial
tipifarnib: CB, drug combination
tipifarnib: DT, drug therapy
retinoid derivative: AE, adverse drug reaction
retinoid derivative: CT, clinical trial
retinoid derivative: CB, drug combination
retinoid derivative: DT, drug therapy
nucleoside analog: AE, adverse drug reaction
nucleoside analog: CT, clinical trial
nucleoside analog: CB, drug combination
nucleoside analog: DT, drug therapy
doxorubicin: AE, adverse drug reaction
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
vincristine: AE, adverse drug reaction
vincristine: CT, clinical trial
vincristine: CB, drug combination
vincristine: DT, drug therapy
etoposide: AE, adverse drug reaction
etoposide: CT, clinical trial
etoposide: CB, drug combination
etoposide: DT, drug therapy
bevacizumab: AE, adverse drug reaction
bevacizumab: CT, clinical trial
bevacizumab: CB, drug combination
bevacizumab: DT, drug therapy
mitoxantrone: AE, adverse drug reaction
mitoxantrone: CT, clinical trial
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
semaxanib: AE, adverse drug reaction
semaxanib: CT, clinical trial
semaxanib: CB, drug combination
semaxanib: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: AE, adverse drug reaction
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CB, drug combination
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
vatalanib: AE, adverse drug reaction
vatalanib: CT, clinical trial
vatalanib: CB, drug combination
vatalanib: DT, drug therapy
rapamycin 2,2 bis(hydroxymethyl)propionate: AE, adverse drug reaction
rapamycin 2,2 bis(hydroxymethyl)propionate: CT, clinical trial
rapamycin 2,2 bis(hydroxymethyl)propionate: CB, drug combination
rapamycin 2,2 bis(hydroxymethyl)propionate: DT, drug therapy
everolimus: AE, adverse drug reaction
everolimus: CT, clinical trial
everolimus: CB, drug combination
everolimus: DT, drug therapy
rapamycin derivative: AE, adverse drug reaction
rapamycin derivative: CT, clinical trial

rapamycin derivative: CB, drug combination
 rapamycin derivative: DT, drug therapy
 ap 23573: AE, adverse drug reaction
 ap 23573: CT, clinical trial
 ap 23573: CB, drug combination
 ap 23573: DT, drug therapy
 arylbutyric acid derivative: AE, adverse drug reaction
 arylbutyric acid derivative: CT, clinical trial
 arylbutyric acid derivative: CB, drug combination
 arylbutyric acid derivative: DT, drug therapy
 unindexed drug
 unclassified drug
 imatinib
 lbh 589

RN (5 aza 2' deoxycytidine) 2353-33-5; (troxacitabine) 145918-75-8; (hydroxyurea) 127-07-1; (daunorubicin) 12707-28-7, 20830-81-3, 23541-50-6; (cytarabine) 147-94-4, 69-74-9; (idarubicin) 57852-57-0, 58957-92-9; (arsenic trioxide) 1303-24-8, 1327-53-3, 13464-58-9, 15502-74-6; (lonafarnib) 193275-84-2; (tipifarnib) 192185-72-1; (doxorubicin) 23214-92-8, 25316-40-9; (vincristine) 57-22-7; (etoposide) 33419-42-0; (bevacizumab) 216974-75-3; (mitoxantrone) 65271-80-9, 70476-82-3; (semaxanib) 186610-95-7; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (vatalanib) 212141-54-3, 212142-18-2; (rapamycin 2,2 bis(hydroxymethyl)propionate) 162635-04-3, 343261-52-9; (everolimus) 159351-69-6; (imatinib) 152459-95-5, 220127-57-1
 CN Sti 571; Sch 66336; R 115777; Su 5416; Su 6668; Ptk 787; Cci 779; Rad 001; Ap 23573; Lbh 589

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 on STN

ACCESSION NUMBER: 2004268142 EMBASE
 TITLE: **Imatinib mesylate** in the treatment of chronic myelogenous leukemia.
 AUTHOR: Borthakur G.; Cortes J.E.
 CORPORATE SOURCE: Dr. J.E. Cortes, Department of Leukemia, Univ. TX M. D. Anderson Cancer Ctr., Box 0428, 1515 Holcombe Blvd, Houston, TX 77030, United States. jcortes@mdanderson.org
 SOURCE: International Journal of Hematology, (2004) 79/5 (411-419). Refs: 69
 ISSN: 0925-5710 CODEN: IJHEEY
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 016 Cancer
 025 Hematology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB **Imatinib mesylate** binds to the inactive conformation of BCR-ABL tyrosine kinase, suppressing the Philadelphia chromosome-positive clone in chronic myelogenous leukemia (CML). Clinical studies of imatinib have yielded impressive results in the treatment of all phases of CML. With the higher rates of complete cytogenetic response with imatinib, molecular monitoring of disease has become mandatory in assessing response and determining prognosis. The practical aspects of the treatment of CML with imatinib are discussed. The emergence of imatinib resistance, albeit in a small percentage of patients, has prompted an evaluation of innovative treatment strategies. .COPYRGT. 2004 The Japanese Society of Hematology.

CT Medical Descriptors:
*chronic myeloid leukemia: DR, drug resistance
*chronic myeloid leukemia: DT, drug therapy
drug binding
enzyme conformation
Philadelphia 1 chromosome
cytogenetics
drug response
drug monitoring
bone marrow suppression: SI, side effect
neutropenia: SI, side effect
thrombocytopenia: SI, side effect
anemia: SI, side effect
cardiotoxicity: SI, side effect
fatigue: SI, side effect
bone pain: DT, drug therapy
bone pain: SI, side effect
liver toxicity: SI, side effect
rash: SI, side effect
nausea: DT, drug therapy
nausea: SI, side effect
vomiting: DT, drug therapy
vomiting: SI, side effect
edema: DT, drug therapy
edema: SI, side effect
muscle cramp: SI, side effect
arthralgia: SI, side effect
diarrhea: DT, drug therapy
diarrhea: SI, side effect
lung edema: DT, drug therapy
lung edema: SI, side effect
drug mechanism
human
clinical trial
review
Drug Descriptors:
*imatinib: AE, adverse drug reaction
*imatinib: CT, clinical trial
*imatinib: CB, drug combination
*imatinib: CM, drug comparison
*imatinib: DT, drug therapy
*imatinib: PD, pharmacology
BCR ABL protein
protein tyrosine kinase inhibitor
interferon: CT, clinical trial
interferon: CB, drug combination
interferon: CM, drug comparison
interferon: DT, drug therapy
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DO, drug dose
cytarabine: DT, drug therapy
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
vincristine: CB, drug combination
vincristine: DT, drug therapy
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
dexamethasone: CB, drug combination

dexamethasone: DT, drug therapy
 prochlorperazine: DT, drug therapy
 omeprazole: DT, drug therapy
 ondansetron: DT, drug therapy
 loperamide: DT, drug therapy
 nonsteroid antiinflammatory agent: DT, drug therapy
 diuretic agent: DT, drug therapy
 tyrphostin: PD, pharmacology
 adaphostin: PD, pharmacology
 protein farnesyltransferase inhibitor: PD, pharmacology
 tipifarnib: PD, pharmacology
 lonafarnib: PD, pharmacology
 5 aza 2' deoxycytidine: DT, drug therapy
 5 aza 2' deoxycytidine: PD, pharmacology
 antineoplastic agent: DT, drug therapy
 antineoplastic agent: PD, pharmacology
 homoharringtonine: CB, drug combination
 homoharringtonine: DV, drug development
troxacitabine: DV, drug development
 proteasome inhibitor: DV, drug development
 geldanamycin: PD, pharmacology
 alpha2a interferon: CB, drug combination
 alpha2a interferon: DT, drug therapy
 alpha2b interferon: CB, drug combination
 alpha2b interferon: DT, drug therapy
 arsenic trioxide: CB, drug combination
 unclassified drug
 peginterferon alpha2a

RN (imatinib) 152459-95-5, 220127-57-1; (cytarabine) 147-94-4,
 69-74-9; (cyclophosphamide) 50-18-0; (vincristine) 57-22-7; (doxorubicin)
 23214-92-8, 25316-40-9; (dexamethasone) 50-02-2; (prochlorperazine)
 58-38-8; (omeprazole) 73590-58-6, 95510-70-6; (ondansetron) 103639-04-9,
 116002-70-1, 99614-01-4; (loperamide) 34552-83-5, 53179-11-6; (tipifarnib)
 192185-72-1; (lonafarnib) 193275-84-2; (5 aza 2' deoxycytidine) 2353-33-5;
 (homoharringtonine) 26833-87-4; **(troxacitabine)**
145918-75-8; (geldanamycin) 30562-34-6; (alpha2a interferon)
 76543-88-9; (alpha2b interferon) 99210-65-8; (arsenic trioxide) 1303-24-8,
 1327-53-3, 13464-58-9, 15502-74-6; (peginterferon alpha2a) 198153-51-4
 CN (1) Pegasys; R115777; Sch66336
 CO (1) Hoffmann La Roche (United States)

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ACCESSION NUMBER: 2004424349 EMBASE
 TITLE: [News from the ASCO 2004 by localizations - Studies in
 phase I].
 ACTUALITE DE L'ASCO 2004 PAR LOCALISATIONS - ETUDES DE
 PHASE I.
 AUTHOR: Zanetta S.
 CORPORATE SOURCE: S. Zanetta, Centre Georges-Francois-Leclerc, 1, rue du Pr
 Marion, F-21000 Dijon, France
 SOURCE: Oncologie, (2004) 6/5 (365-368).
 ISSN: 1292-3818 CODEN: OOLFG
 COUNTRY: France
 DOCUMENT TYPE: Journal; Conference Article
 FILE SEGMENT: 016 Cancer
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: French
 CT Medical Descriptors:

*cancer chemotherapy
bone marrow suppression: SI, side effect
neutropenia: SI, side effect
thrombocytopenia: SI, side effect
infection: SI, side effect
fatigue: SI, side effect
neurotoxicity: SI, side effect
malaise: SI, side effect
febrile neutropenia: SI, side effect
diarrhea: SI, side effect
chemotherapy induced emesis: SI, side effect
sepsis: SI, side effect
abdominal pain: SI, side effect
constipation: SI, side effect
anemia: SI, side effect
drug hypersensitivity: SI, side effect
liver dysfunction: SI, side effect
hyperglycemia: SI, side effect
dehydration: SI, side effect
hyponatremia: SI, side effect
rash: SI, side effect
skin toxicity: SI, side effect
mucosa inflammation: SI, side effect
peripheral neuropathy: SI, side effect
stomatitis: SI, side effect
hypertension: SI, side effect
thrombosis: SI, side effect
insomnia: SI, side effect
hypokalemia: SI, side effect
kidney failure: SI, side effect
respiration depression: SI, side effect
blood toxicity: SI, side effect
side effect: SI, side effect
urticaria: SI, side effect
hypovolemia: SI, side effect
hypotension: SI, side effect
edema: SI, side effect
human
conference paper
Drug Descriptors:
lapatinib: AE, adverse drug reaction
histone deacetylase inhibitor: AE, adverse drug reaction
indisulam: AE, adverse drug reaction
indisulam: IV, intravenous drug administration
 troxacitabine: AE, adverse drug reaction
 troxacitabine: IV, intravenous drug administration
nucleoside analog: AE, adverse drug reaction
nucleoside analog: IV, intravenous drug administration
exatecan: AE, adverse drug reaction
exatecan: IV, intravenous drug administration
paclitaxel: AE, adverse drug reaction
paclitaxel: IV, intravenous drug administration
ixabepilone: AE, adverse drug reaction
ixabepilone: IV, intravenous drug administration
imatinib: AE, adverse drug reaction
imatinib: CB, drug combination
gefitinib: AE, adverse drug reaction
gefitinib: CB, drug combination
erlotinib: AE, adverse drug reaction
erlotinib: CB, drug combination

n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6
 quinazolinyl]acrylamide: AE, adverse drug reaction
 n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6
 quinazolinyl]acrylamide: CB, drug combination
 3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: AE, adverse drug reaction
 3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4
 isothiazolecarboxamide: CB, drug combination
 vatalanib: AE, adverse drug reaction
 vatalanib: CB, drug combination
 7 hydroxystaurosporine: AE, adverse drug reaction
 7 hydroxystaurosporine: CB, drug combination
 gene expression modulator 231: AE, adverse drug reaction
 gene expression modulator 231: CB, drug combination
 bortezomib: AE, adverse drug reaction
 bortezomib: CB, drug combination
 lonafarnib: AE, adverse drug reaction
 lonafarnib: CB, drug combination
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
 thienylsulfonyl) 1h 1,4 benzodiazepine: AE, adverse drug reaction
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
 thienylsulfonyl) 1h 1,4 benzodiazepine: CB, drug combination
 everolimus: AE, adverse drug reaction
 tariquidar: AE, adverse drug reaction
 tariquidar: CB, drug combination
 elacridar: AE, adverse drug reaction
 elacridar: CB, drug combination
 retinoid: AE, adverse drug reaction
 epothilone B: AE, adverse drug reaction
 epothilone B: IV, intravenous drug administration
 discodermolide: AE, adverse drug reaction
 discodermolide: PO, oral drug administration
 taxane derivative: AE, adverse drug reaction
 taxane derivative: PO, oral drug administration
 alkylating agent: AE, adverse drug reaction
 alkylating agent: IV, intravenous drug administration
 DNA topoisomerase inhibitor: AE, adverse drug reaction
 DNA topoisomerase inhibitor: IV, intravenous drug administration
 docetaxel: CB, drug combination
 unindexed drug
 cp 4055
 vnp 40101m
 XK 469
 mac 321
 ai 850
 bms 275183
 dj 927
 kos 906
 t 138067
 abt 751
 xaa 296a
 sb 715992
 emd 72000
 ag 2037
 mbt 0206
 bay 439006
 abt 510
 RN (lapatinib) 388082-78-8, 437755-78-7; (indisulam) 165668-41-7; (
 troxacitabine) 145918-75-8; (exatecan) 197720-53-9;
 (paclitaxel) 33069-62-4; (ixabepilone) 219989-84-1; (imatinib)

152459-95-5, 220127-57-1; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (erlotinib) 183319-69-9, 183321-74-6; (n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6 quinazolinyl]acrylamide) 267243-28-7, 338796-35-3; (3 (4 bromo 2,6 difluorobenzyloxy) 5 [3 [4 (1 pyrrolidinyl)butyl]ureido] 4 isothiazolecarboxamide) 252003-65-9; (vatalanib) 212141-54-3, 212142-18-2; (7 hydroxystaurosporine) 112953-11-4; (bortezomib) 179324-69-7, 197730-97-5; (lonafarnib) 193275-84-2; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (everolimus) 159351-69-6; (tariquidar) 206873-63-4; (elacridar) 143664-11-3; (epothilone B) 152044-54-7; (discodermolide) 127943-53-7, 154335-30-5, 194232-29-6; (docetaxel) 114977-28-5

CN Gw 572016; Cp 4055; Dx 8951f; E 7070; Bms 247550; Abi 007; **Gleevec** ; Zd 1839; Osi 774; Ci 1033; Cp 547632; Ptk 787; Zk 222584; Ucn 01; GEM 231; Sch 66336; Bms 214662; Rad 001; Vnp 40101m; XK 469; Mac 321; Ai 850; Bms 275183; Dj 927; Epo 906; Kos 906; T 138067; Abt 751; Xaa 296a; Sb 715992; Emd 72000; Ag 2037; Mbt 0206; Bay 439006; Abt 510

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ACCESSION NUMBER: 2004165534 EMBASE
TITLE: Novel therapies for patients with chronic myeloid leukemia.
AUTHOR: Giles F.J.; Kantarjian H.; Cortes J.
CORPORATE SOURCE: Dr. F.J. Giles, Department of Leukemia, University of Texas, MD Anderson Cancer Center, 1400 Holcombe Boulevard, Houston, TX 77030, United States. frankgiles@aol.com
SOURCE: Expert Review of Anticancer Therapy, (2004) 4/2 (271-282).
Refs: 177
ISSN: 1473-7140 CODEN: ERATBJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The most immediate issues that will have a major impact on the long-term survival of patients with chronic myeloid leukemia is the optimal use of **imatinib mesylate (Gleevec.RTM., Novartis)** and the development of effective therapies for those patients who are intolerant of, or become resistant to, optimal doses of this agent. Of the multiple new agents that are currently being developed for patients with chronic myeloid leukemia, most are being investigated in patients who have developed resistance to imatinib, which is a confounding factor in itself. The mechanisms of action of novel agents are diverse and they may have a variably synergistic therapeutic relationship with imatinib. The complete blockade of the intracellular pathways that are triggered by Bcr-Abl, combined with successful reversal of apoptotic and/or angiogenic abnormalities in chronic myeloid leukemia, may well lead to a cure for the majority of patients. .COPYRGHT. Future Drugs Ltd. All rights reserved.

CT Medical Descriptors:
*chronic myeloid leukemia: DR, drug resistance
*chronic myeloid leukemia: DT, drug therapy
survival time
drug use
drug research
drug efficacy
drug hypersensitivity: SI, side effect

cancer resistance
optimal drug dose
drug mechanism
drug potentiation
apoptosis
angiogenesis
cancer patient
dose response
DNA methylation
bone marrow suppression: SI, side effect
fever: SI, side effect
drug metabolism
human
nonhuman
clinical trial
review

Drug Descriptors:

*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: DV, drug development
*antineoplastic agent: DO, drug dose
*antineoplastic agent: IT, drug interaction
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PK, pharmacokinetics
*antineoplastic agent: PD, pharmacology
*antineoplastic agent: IV, intravenous drug administration
*antineoplastic agent: PO, oral drug administration
imatinib: AE, adverse drug reaction
imatinib: CT, clinical trial
imatinib: CB, drug combination
imatinib: CM, drug comparison
imatinib: DO, drug dose
imatinib: IT, drug interaction
imatinib: DT, drug therapy
imatinib: PD, pharmacology
BCR ABL protein: EC, endogenous compound
alpha interferon: CT, clinical trial
alpha interferon: CB, drug combination
alpha interferon: CM, drug comparison
alpha interferon: DT, drug therapy
alpha interferon: PD, pharmacology
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DT, drug therapy
cytarabine: PK, pharmacokinetics
cytarabine: PD, pharmacology
azacitidine: CB, drug combination
azacitidine: DT, drug therapy
azacitidine: PD, pharmacology
5 aza 2' deoxycytidine: AE, adverse drug reaction
5 aza 2' deoxycytidine: CB, drug combination
5 aza 2' deoxycytidine: DO, drug dose
5 aza 2' deoxycytidine: IT, drug interaction
5 aza 2' deoxycytidine: DT, drug therapy
5 aza 2' deoxycytidine: PD, pharmacology
etoposide: CB, drug combination
etoposide: DT, drug therapy

etoposide: PD, pharmacology
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
mitoxantrone: PD, pharmacology
histone deacetylase inhibitor: CB, drug combination
histone deacetylase inhibitor: IT, drug interaction
histone deacetylase inhibitor: DT, drug therapy
histone deacetylase inhibitor: PD, pharmacology
suberoylanilide hydroxamic acid: CB, drug combination
suberoylanilide hydroxamic acid: IT, drug interaction
suberoylanilide hydroxamic acid: DT, drug therapy
suberoylanilide hydroxamic acid: PD, pharmacology
depsipeptide: PD, pharmacology
hydroxamic acid derivative: PD, pharmacology
4 [n (2 hydroxyethyl) n [2 (3 indolyl)ethyl]aminomethyl]cinnamohydroxamic
acid: PD, pharmacology
protein p21: EC, endogenous compound
protein p27: EC, endogenous compound
vasculotropin: EC, endogenous compound
bevacizumab: CB, drug combination
bevacizumab: DT, drug therapy
bevacizumab: PD, pharmacology
vasculotropin antibody: CB, drug combination
vasculotropin antibody: DT, drug therapy
vasculotropin antibody: PD, pharmacology
monoclonal antibody: CB, drug combination
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
 protein tyrosine kinase inhibitor: CT, clinical trial
 protein tyrosine kinase inhibitor: CB, drug combination
 protein tyrosine kinase inhibitor: DO, drug dose
 protein tyrosine kinase inhibitor: DT, drug therapy
 protein tyrosine kinase inhibitor: PD, pharmacology
 protein tyrosine kinase inhibitor: IV, intravenous drug
administration
 protein tyrosine kinase inhibitor: PO, oral drug administration
ag 013736: CT, clinical trial
ag 013736: DT, drug therapy
ag 013736: PD, pharmacology
vatalanib: CT, clinical trial
vatalanib: CB, drug combination
vatalanib: DT, drug therapy
vatalanib: PD, pharmacology
vatalanib: PO, oral drug administration
n benzoylstauropine: DT, drug therapy
n benzoylstauropine: PD, pharmacology
semaxanib: DO, drug dose
semaxanib: DT, drug therapy
semaxanib: PD, pharmacology
semaxanib: IV, intravenous drug administration
phthalazine derivative: CT, clinical trial
phthalazine derivative: CB, drug combination
phthalazine derivative: DT, drug therapy
phthalazine derivative: PD, pharmacology
phthalazine derivative: PO, oral drug administration
troxacitabine: CT, clinical trial
troxacitabine: CB, drug combination
troxacitabine: CM, drug comparison
troxacitabine: DT, drug therapy
troxacitabine: PK, pharmacokinetics

troxacitabine: PD, pharmacology
 lamivudine: PD, pharmacology
 deoxycytidine kinase: EC, endogenous compound
 unindexed drug
 unclassified drug

RN (imatinib) 152459-95-5, 220127-57-1; (cytarabine) 147-94-4,
 69-74-9; (azacitidine) 320-67-2, 52934-49-3; (5 aza 2' deoxycytidine)
 2353-33-5; (etoposide) 33419-42-0; (mitoxantrone) 65271-80-9, 70476-82-3;
 (protein p21) 85306-28-1; (vasculotropin) 127464-60-2; (bevacizumab)
 216974-75-3; (vatalanib) 212141-54-3, 212142-18-2; (n
 benzoylstauroporine) 120685-11-2; (semaxanib) 186610-95-7; (
 troxacitabine) 145918-75-8; (lamivudine) 134678-17-4,
 134680-32-3; (deoxycytidine kinase) 9039-45-6
 CN (1) Gleevec; (2) Sti 571; (3) Avastin; Laq 824; Ptk
 787; Pkc 412; Su 5416; Ag 013736
 CO (2) Novartis; (3) Genentech

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ACCESSION NUMBER: 2003396846 EMBASE
 TITLE: Phase 2 clinical and pharmacologic study of clofarabine in
 patients with refractory or relapsed acute leukemia.
 AUTHOR: Kantarjian H.; Gandhi V.; Cortes J.; Verstovsek S.; Du M.;
 Garcia-Manero G.; Giles F.; Faderl S.; O'Brien S.; Jeha S.;
 Davis J.; Shaked Z.; Craig A.; Keating M.; Plunkett W.;
 Freireich E.J.
 CORPORATE SOURCE: H. Kantarjian, Department of Leukemia, Box 428, Univ. Texas
 MD Anderson Cancer Ctr., 1515 Holcombe Blvd, Houston, TX
 77030, United States. hkantarj@mdanderson.org
 SOURCE: Blood, (1 Oct 2003) 102/7 (2379-2386).
 Refs: 40
 ISSN: 0006-4971 CODEN: BLOOAW
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 016 Cancer
 025 Hematology
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB In a phase 2 study, 62 patients with relapsed and refractory acute myeloid
 leukemia (AML; n = 31), myelodysplastic syndrome (MDS; n = 8), chronic
 myeloid leukemia in blastic phase (CMLBP; n = 11), and acute lymphocytic
 leukemia (ALL; n = 12) received 40 mg/m² clofarabine intravenously over
 1 hour daily for 5 days, every 3 to 6 weeks. Twenty patients (32%)
 achieved complete response (CR), 1 had a partial response (PR), and 9
 (15%) achieved CR but without platelet recovery (CRp), for an overall
 response rate of 48%. In AML, responses were noted in 2 (18%) of 11
 patients in first salvage with short first CR (\leq 12 months), in 7
 (87%) of 8 patients with longer first CR, and in 8 (67%) of 12 patients in
 second or subsequent salvage. Responses were observed in 4 of 8 patients
 with high-risk MDS (50%), in 7 (64%) of 11 with CML-BP, and in 2 (17%) of
 12 with ALL. Severe reversible liver dysfunction was noted in 15% to 25%.
 After the first clofarabine infusion, responders accumulated more
 clofarabine triphosphate in blasts compared with nonresponders (median 18
 vs 10 μ M; P = .03). This increased only in responders (median,
 1.8-fold; P = .008) after the second clofarabine infusion. In summary,
 clofarabine is active in acute leukemias and MDS; cellular
 pharmacokinetics may have prognostic significance. .COPYRGT. 2003 by The

American Society of Hematology.
CT Medical Descriptors:
*cancer recurrence
*acute granulocytic leukemia: DT, drug therapy
*myelodysplastic syndrome: DT, drug therapy
*chronic myeloid leukemia: DT, drug therapy
*acute lymphocytic leukemia: DT, drug therapy
thrombocyte count
drug response
salvage therapy
high risk population
disease severity
liver dysfunction: SI, side effect
drug infusion
blast cell
prognosis
drug mechanism
treatment outcome
drug blood level
rash: SI, side effect
hand foot syndrome: SI, side effect
mucosa inflammation: SI, side effect
drug fatality: SI, side effect
diarrhea: SI, side effect
nausea: SI, side effect
vomiting: SI, side effect
drug half life
blood toxicity: SI, side effect
infection: SI, side effect
sepsis: SI, side effect
human
male
female
major clinical study
clinical trial
phase 2 clinical trial
controlled study
aged
adult
article
priority journal
Drug Descriptors:
*nucleoside derivative: AE, adverse drug reaction
*nucleoside derivative: CT, clinical trial
*nucleoside derivative: CR, drug concentration
*nucleoside derivative: DT, drug therapy
*nucleoside derivative: PK, pharmacokinetics
*nucleoside derivative: PD, pharmacology
*nucleoside derivative: IV, intravenous drug administration
*clofarabine: AE, adverse drug reaction
*clofarabine: CT, clinical trial
*clofarabine: CR, drug concentration
*clofarabine: DT, drug therapy
*clofarabine: PK, pharmacokinetics
*clofarabine: PD, pharmacology
*clofarabine: IV, intravenous drug administration
thalidomide: DT, drug therapy
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
cytarabine: CB, drug combination

cytarabine: DT, drug therapy
 topotecan: CB, drug combination
 topotecan: DT, drug therapy
 granulocyte colony stimulating factor: CB, drug combination
 granulocyte colony stimulating factor: DT, drug therapy
 imatinib: CB, drug combination
 imatinib: DT, drug therapy
 gemtuzumab ozogamicin: CB, drug combination
 gemtuzumab ozogamicin: DT, drug therapy
 troxacitabine: CB, drug combination
 troxacitabine: DT, drug therapy
 prednisone: CB, drug combination
 prednisone: DT, drug therapy
 vincristine: CB, drug combination
 vincristine: DT, drug therapy
 daunorubicin: CB, drug combination
 daunorubicin: DT, drug therapy
 doxorubicin: CB, drug combination
 doxorubicin: DT, drug therapy
 dexamethasone: CB, drug combination
 dexamethasone: DT, drug therapy
 mitoxantrone: CB, drug combination
 mitoxantrone: DT, drug therapy
 alpha interferon: DT, drug therapy
 unclassified drug

RN (thalidomide) 50-35-1; (cyclophosphamide) 50-18-0; (cytarabine) 147-94-4,
 69-74-9; (topotecan) 119413-54-6, 123948-87-8; (imatinib) 152459-95-5,
 220127-57-1; (**troxacitabine**) **145918-75-8**;
 (prednisone) 53-03-2; (vincristine) 57-22-7; (daunorubicin) 12707-28-7,
 20830-81-3, 23541-50-6; (doxorubicin) 23214-92-8, 25316-40-9;
 (dexamethasone) 50-02-2; (mitoxantrone) 65271-80-9, 70476-82-3
 CO Ash Stevens (United States)

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ACCESSION NUMBER: 2003175598 EMBASE
 TITLE: Perspectives on the treatment of chronic phase and advanced
 phase CML and Philadelphia chromosome positive ALL.
 AUTHOR: Schiffer C.A.; Hehlmann R.; Larson R.
 CORPORATE SOURCE: C.A. Schiffer, Division of Hematology and Oncology,
 Karmanos Cancer Institute, Wayne State Univ. School of
 Medicine, 505 Hudson 3990 John R, Detroit, MI 48201, United
 States
 SOURCE: Leukemia, (1 Apr 2003) 17/4 (691-699).
 Refs: 73
 ISSN: 0887-6924 CODEN: LEUKED
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 016 Cancer
 022 Human Genetics
 025 Hematology
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles

LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Chronic myeloid leukaemia (CML) is a malignant disease of the bone marrow
 characterised by the presence of the Philadelphia (Ph) chromosome. About
 20% of acute lymphoblastic leukaemia (ALL) patients also show this genetic
 abnormality. A new drug, imatinib (**Glivec**.RTM., Novartis Pharma

AG, Basel, Switzerland, and formerly STI571) is having a profound effect on the treatment and management of all stages of CML and Philadelphia chromosome positive (Ph+) ALL. New treatment algorithms are being developed. Should imatinib replace or be combined with existing therapies? To address this question, we review the pros and cons of therapy with interferon- α (IFN- α), allogeneic transplantation, autologous transplantation, imatinib, and in the case of Ph+ ALL, chemotherapy and experimental approaches. Conservative and aggressive treatments will be discussed and new molecular methods of monitoring cytogenetic response and their significance will also be reviewed.

CT Medical Descriptors:

- *chronic myeloid leukemia: DR, drug resistance
- *chronic myeloid leukemia: DT, drug therapy
- *chronic myeloid leukemia: RT, radiotherapy
- *chronic myeloid leukemia: TH, therapy
- *acute lymphoblastic leukemia: DT, drug therapy
- *acute lymphoblastic leukemia: TH, therapy
- *Philadelphia 1 chromosome
- advanced cancer: DR, drug resistance
- advanced cancer: DT, drug therapy
- advanced cancer: TH, therapy
- bone marrow cancer: DR, drug resistance
- bone marrow cancer: DT, drug therapy
- bone marrow cancer: RT, radiotherapy
- bone marrow cancer: TH, therapy
- clinical feature
- genetic disorder: DR, drug resistance
- genetic disorder: DT, drug therapy
- genetic disorder: RT, radiotherapy
- genetic disorder: TH, therapy
- drug effect
- cancer staging
- algorithm
- allogenic bone marrow transplantation
- autologous bone marrow transplantation
- cancer combination chemotherapy
- conservative treatment
- methodology
- patient monitoring
- cytogenetics
- treatment outcome
- drug indication
- dose response
- withdrawal syndrome: SI, side effect
- cancer radiotherapy
- cancer resistance
- diarrhea: SI, side effect
- nausea and vomiting: SI, side effect
- fluid retention
- blood toxicity: SI, side effect
- human
- clinical trial
- article
- priority journal
- Drug Descriptors:
- *imatinib: AE, adverse drug reaction
- *imatinib: CT, clinical trial
- *imatinib: CB, drug combination
- *imatinib: CM, drug comparison
- *imatinib: DO, drug dose

*imatinib: DT, drug therapy
*imatinib: PD, pharmacology
alpha interferon: AE, adverse drug reaction
alpha interferon: CT, clinical trial
alpha interferon: CB, drug combination
alpha interferon: CM, drug comparison
alpha interferon: DO, drug dose
alpha interferon: DT, drug therapy
alpha interferon: PD, pharmacology
hydroxyurea: CB, drug combination
hydroxyurea: CM, drug comparison
hydroxyurea: DT, drug therapy
hydroxyurea: PD, pharmacology
protein tyrosine kinase inhibitor: DT, drug therapy
protein tyrosine kinase inhibitor: PD, pharmacology
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: CT, clinical trial
antineoplastic agent: CB, drug combination
antineoplastic agent: CM, drug comparison
antineoplastic agent: DO, drug dose
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
busulfan: CB, drug combination
busulfan: DT, drug therapy
cytarabine: AE, adverse drug reaction
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DT, drug therapy
cytarabine: PD, pharmacology
anthracycline: AE, adverse drug reaction
anthracycline: CB, drug combination
anthracycline: DT, drug therapy
anthracycline: PD, pharmacology
cladribine: DO, drug dose
cladribine: DT, drug therapy
cladribine: PD, pharmacology
purine derivative: DO, drug dose
purine derivative: DT, drug therapy
purine derivative: PD, pharmacology
5 aza 2' deoxycytidine: DT, drug therapy
5 aza 2' deoxycytidine: PD, pharmacology
pyrimidine derivative: DT, drug therapy
pyrimidine derivative: PD, pharmacology
troxacitabine: DT, drug therapy
troxacitabine: PD, pharmacology
nucleoside analog: DT, drug therapy
nucleoside analog: PD, pharmacology
antibody conjugate: DT, drug therapy
antibody conjugate: PD, pharmacology
gemtuzumab ozogamicin: CB, drug combination
gemtuzumab ozogamicin: DT, drug therapy
gemtuzumab ozogamicin: PD, pharmacology
protein farnesyltransferase inhibitor: CB, drug combination
protein farnesyltransferase inhibitor: DT, drug therapy
protein farnesyltransferase inhibitor: PD, pharmacology
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
cyclophosphamide: PD, pharmacology
vincristine: CB, drug combination
vincristine: DT, drug therapy

vincristine: PD, pharmacology
 doxorubicin: CB, drug combination
 doxorubicin: DT, drug therapy
 doxorubicin: PD, pharmacology
 dexamethasone: CB, drug combination
 dexamethasone: DT, drug therapy
 dexamethasone: PD, pharmacology
 methotrexate: CB, drug combination
 methotrexate: DO, drug dose
 methotrexate: DT, drug therapy
 methotrexate: PD, pharmacology
 RN (imatinib) 152459-95-5, **220127-57-1**; (hydroxyurea) 127-07-1;
 (busulfan) 55-98-1; (cytarabine) 147-94-4, 69-74-9; (cladribine)
 4291-63-8; (5 aza 2' deoxycytidine) 2353-33-5; (**troxacitabine**)
145918-75-8; (cyclophosphamide) 50-18-0; (vincristine) 57-22-7;
 (doxorubicin) 23214-92-8, 25316-40-9; (dexamethasone) 50-02-2;
 (methotrexate) 15475-56-6, 59-05-2, 7413-34-5
 CN (1) **Glivec**; (2) **Sti 571**; (3) Mylotarg
 CO (2) Novartis (Switzerland); (3) Wyeth (United States)

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ACCESSION NUMBER: 2003165547 EMBASE
 TITLE: New antileukemic agents.
 AUTHOR: Mantadakis E.; Kalmanti M.
 CORPORATE SOURCE: Dr. M. Kalmanti, Pediatric Hematology/Oncology Clinic,
 University Hospital of Heraklion, 71 110 Heraklion, Crete,
 Greece. pedhem@med.uoc.gr
 SOURCE: Pediatric Hematology and Oncology, (2003) 20/3 (173-185).
 Refs: 70
 ISSN: 0888-0018 CODEN: PHONEN
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review
 FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
 016 Cancer
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Despite the tremendous progress in the treatment of childhood leukemias over the last 50 years, certain subgroups of children continue to have poor prognosis. Hence, there is a need for development of new antileukemic agents. In this review, the authors describe results of clinical trials of several new antileukemic compound with different mechanisms of action (signal transduction inhibitors, nucleoside analogs, DNA hypomethylators, angiogenesis inhibitors, and monoclonal antibodies). Although most of these compounds are not used in pediatric leukemias, the concepts surrounding their clinical development are important to all pediatric hematologists/oncologists.

CT Medical Descriptors:
 *childhood leukemia: DR, drug resistance
 *childhood leukemia: DT, drug therapy
 *childhood leukemia: TH, therapy
 *cancer chemotherapy
 prognosis
 drug mechanism
 signal transduction
 DNA methylation
 treatment outcome

chronic myeloid leukemia: DT, drug therapy
malignant transformation
antineoplastic activity
acute lymphoblastic leukemia: DT, drug therapy
hematopoietic stem cell transplantation
blood toxicity: SI, side effect
liver dysfunction: SI, side effect
gene mutation
oncogene ras
side effect: SI, side effect
drug efficacy
stomatitis: SI, side effect
hand foot syndrome: SI, side effect
skin manifestation: SI, side effect
desquamation: SI, side effect
pruritus: SI, side effect
bone marrow suppression: SI, side effect
drug eruption: SI, side effect
drug half life
drug clearance
drug blood level
drug solubility
neurotoxicity: SI, side effect
pancytopenia: SI, side effect
anemia: SI, side effect
neutropenia: SI, side effect
thrombocytopenia: SI, side effect
liver toxicity: SI, side effect
mucosa inflammation: SI, side effect
hyperbilirubinemia: SI, side effect
human
clinical trial
review

Drug Descriptors:

*antileukemic agent: AE, adverse drug reaction
*antileukemic agent: CT, clinical trial
*antileukemic agent: CR, drug concentration
*antileukemic agent: DO, drug dose
*antileukemic agent: DT, drug therapy
*antileukemic agent: PR, pharmaceuticals
*antileukemic agent: PK, pharmacokinetics
*antileukemic agent: PD, pharmacology
*antileukemic agent: IV, intravenous drug administration
nucleoside derivative: AE, adverse drug reaction
nucleoside derivative: CT, clinical trial
nucleoside derivative: CR, drug concentration
nucleoside derivative: DO, drug dose
nucleoside derivative: DT, drug therapy
nucleoside derivative: PR, pharmaceuticals
nucleoside derivative: PK, pharmacokinetics
nucleoside derivative: PD, pharmacology
nucleoside derivative: IV, intravenous drug administration
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PD, pharmacology
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: CT,
clinical trial
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: DT,
drug therapy
3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one: PD,

pharmacology
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
monoclonal antibody: AE, adverse drug reaction
monoclonal antibody: CT, clinical trial
monoclonal antibody: CB, drug combination
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
monoclonal antibody: IV, intravenous drug administration
aletuzumab: AE, adverse drug reaction
aletuzumab: CT, clinical trial
aletuzumab: DT, drug therapy
aletuzumab: PD, pharmacology
aletuzumab: IV, intravenous drug administration
gemtuzumab ozogamicin: AE, adverse drug reaction
gemtuzumab ozogamicin: CT, clinical trial
gemtuzumab ozogamicin: DT, drug therapy
gemtuzumab ozogamicin: PD, pharmacology
protein kinase inhibitor: AE, adverse drug reaction
protein kinase inhibitor: CT, clinical trial
protein kinase inhibitor: DO, drug dose
protein kinase inhibitor: DT, drug therapy
protein kinase inhibitor: PD, pharmacology
1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine: PD, pharmacology
pyrrole derivative: PD, pharmacology
imatinib: AE, adverse drug reaction
imatinib: CT, clinical trial
imatinib: DO, drug dose
imatinib: DT, drug therapy
imatinib: PD, pharmacology
interferon: DT, drug therapy
Flt3 ligand: EC, endogenous compound
n benzoylstauroporine: PD, pharmacology
protein farnesyltransferase inhibitor: CT, clinical trial
protein farnesyltransferase inhibitor: DT, drug therapy
protein farnesyltransferase inhibitor: PD, pharmacology
protein farnesyltransferase inhibitor: PO, oral drug administration
r 115777: CT, clinical trial
r 115777: DT, drug therapy
r 115777: PD, pharmacology
r 115777: PO, oral drug administration
troxacitabine: AE, adverse drug reaction
troxacitabine: CB, drug combination
troxacitabine: CM, drug comparison
troxacitabine: CR, drug concentration
troxacitabine: DO, drug dose
troxacitabine: DT, drug therapy
fludarabine: DT, drug therapy
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DT, drug therapy
nelarabine: AE, adverse drug reaction
nelarabine: CT, clinical trial
nelarabine: CM, drug comparison
nelarabine: PR, pharmaceuticals
nelarabine: PK, pharmacokinetics

nelarabine: PD, pharmacology
 nelarabine: IV, intravenous drug administration
 guanine arabinoside: CM, drug comparison
 guanine arabinoside: CR, drug concentration
 5 aza 2' deoxycytidine: AE, adverse drug reaction
 5 aza 2' deoxycytidine: CT, clinical trial
 5 aza 2' deoxycytidine: DT, drug therapy
 5 aza 2' deoxycytidine: PD, pharmacology
 unclassified drug
 zarnestra
 semixanib
 pk 1166
 pkc 412
 506u78

RN (3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one)
 186610-95-7; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3
 pyrrolepropionic acid) 252916-29-3; (1 (4 chloroanilino) 4 (4
 pyridylmethyl)phthalazine) 212142-18-2; (imatinib) 152459-95-5,
 220127-57-1; (Flt3 ligand) 171404-15-2; (n benzoylstauroporine)
 120685-11-2; (**troxacitabine**) 145918-75-8;
 (fludarabine) 21679-14-1; (cytarabine) 147-94-4, 69-74-9; (guanine
 arabinoside) 38819-10-2; (5 aza 2' deoxycytidine) 2353-33-5
 CN (1) R 115777; (2) Zarnestra; (3) Su 5416; (4) Semixanib; Pk 1166; Ptk 787;
 Zk 222584; St 1571; Pkc 412; **Bch 4556**; 506u78; Su 6668
 CO (2) Janssen Ortho; (4) Sugen (United States)

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ACCESSION NUMBER: 2002047444 EMBASE
 TITLE: Phase II study of **troxacitabine**, a novel
 dioxolane nucleoside analog, in patients with refractory
 leukemia.
 AUTHOR: Giles F.J.; Garcia-Manero G.; Cortes J.E.; Baker S.D.;
 Miller C.B.; O'Brien S.M.; Thomas D.A.; Andreeff M.; Bivins
 C.; Jolivet J.; Kantarjian H.M.
 CORPORATE SOURCE: Dr. F.J. Giles, University of Texas, M.D. Anderson Cancer
 Center, Department of Leukemia, 1400 Holcombe Blvd,
 Houston, TX 77030, United States. fgiles@mdanderson.org
 SOURCE: Journal of Clinical Oncology, (1 Feb 2002) 20/3 (656-664).
 Refs: 43
 ISSN: 0732-183X CODEN: JCONDN
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 016 Cancer
 025 Hematology
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Purpose: To investigate the activity of a novel dioxolane L-nucleoside
 analog, **troxacitabine** (L-(-)-OddC, **BCH-4556**
), in patients with refractory leukemia. Patients and Methods: Study
 participants were patients with refractory or relapsed acute myeloid (AML)
 or lymphocytic (ALL) leukemia, myelodysplastic syndromes (MDS), or chronic
 myelogenous leukemia in blastic phase (CML-BP). **Troxacitabine**
 was provided as an intravenous infusion for more than 30 minutes daily for
 5 days at a dose of 8.0 mg/m(2)/d (40 mg/m(2) per course). Courses were
 given every 3 to 4 weeks according to antileukemic efficacy. Results:
 Forty-two patients (AML, 18 patients; MDS, one patient; ALL, six patients;

CML-BP, 17 patients) were treated. Median age was 51 years (range, 23 to 80 years); 22 patients were male. Stomatitis was the most significant adverse event, with three patients (7%) and two patients (5%), respectively, experiencing grade 3 or 4 toxicity. Ten patients (24%) had grade 3 hand-foot syndrome, and two patients (5%) had grade 3 skin rash. One patient (2%) had grade 3 fatigue and anorexia. Marrow hypoplasia occurred between days 14 and 28 in 12 (75%) of 16 assessable patients with AML. Two complete remissions and one partial remission (18%) were observed in 16 assessable patients with AML. None of six patients with ALL responded. Six (37%) of 16 assessable patients with CML-BP experienced a return to chronic-phase disease. Conclusion: **Troxacitabine** has significant antileukemic activity in patients with AML and CML-BP. .COPYRG. 2002 by American Society of Clinical Oncology.

CT Medical Descriptors:

- *leukemia: DT, drug therapy
- *cancer recurrence: DT, drug therapy
- acute granulocytic leukemia: DT, drug therapy
- lymphatic leukemia: DT, drug therapy
- myelodysplastic syndrome: DT, drug therapy
- chronic myeloid leukemia: DT, drug therapy
- blast cell crisis: DT, drug therapy
- drug efficacy
- antineoplastic activity
- stomatitis: SI, side effect
- hand foot syndrome: SI, side effect
- rash: SI, side effect
- fatigue: SI, side effect
- anorexia: SI, side effect
- bone marrow hypoplasia: SI, side effect
- disease severity
- cancer regression
- chronic disease
- area under the curve
- human
- male
- female
- clinical article
- clinical trial
- phase 2 clinical trial
- aged
- adult
- article
- priority journal

Drug Descriptors:

- *troxacitabine: AE, adverse drug reaction
- *troxacitabine: CT, clinical trial
- *troxacitabine: AN, drug analysis
- *troxacitabine: CR, drug concentration
- *troxacitabine: DO, drug dose
- *troxacitabine: DT, drug therapy
- *troxacitabine: PK, pharmacokinetics
- *troxacitabine: IV, intravenous drug administration
- *1,3 dioxolane derivative: AE, adverse drug reaction
- *1,3 dioxolane derivative: CT, clinical trial
- *1,3 dioxolane derivative: AN, drug analysis
- *1,3 dioxolane derivative: CR, drug concentration
- *1,3 dioxolane derivative: DO, drug dose
- *1,3 dioxolane derivative: DT, drug therapy
- *1,3 dioxolane derivative: PK, pharmacokinetics
- *1,3 dioxolane derivative: IV, intravenous drug administration

*nucleoside analog: AE, adverse drug reaction
 *nucleoside analog: CT, clinical trial
 *nucleoside analog: AN, drug analysis
 *nucleoside analog: CR, drug concentration
 *nucleoside analog: DO, drug dose
 *nucleoside analog: DT, drug therapy
 *nucleoside analog: PK, pharmacokinetics
 *nucleoside analog: IV, intravenous drug administration

deoxycytidine: AN, drug analysis

cytarabine: AN, drug analysis

fludarabine: AN, drug analysis

cladribine

cyclophosphamide

topotecan

tioguanine

daunorubicin

mitoxantrone

imatinib

idarubicin

etoposide

vincristine

dexamethasone

clofarabine

5 aza 2' deoxycytidine

hydroxyurea

busulfan

homoharringtonine

thymocyte antibody

tallimustine

methotrexate

alpha interferon

unclassified drug

RN (troxacitabine) 145918-75-8; (deoxycytidine) 951-77-9;
 (cytarabine) 147-94-4, 69-74-9; (fludarabine) 21679-14-1; (cladribine)
 4291-63-8; (cyclophosphamide) 50-18-0; (topotecan) 119413-54-6,
 123948-87-8; (tioguanine) 154-42-7; (daunorubicin) 12707-28-7, 20830-81-3,
 23541-50-6; (mitoxantrone) 65271-80-9, 70476-82-3; (imatinib) 152459-95-5,
 220127-57-1; (idarubicin) 57852-57-0, 58957-92-9; (etoposide)
 33419-42-0; (vincristine) 57-22-7; (dexamethasone) 50-02-2; (5 aza 2'
 deoxycytidine) 2353-33-5; (hydroxyurea) 127-07-1; (busulfan) 55-98-1;
 (homoharringtonine) 26833-87-4; (tallimustine) 115308-98-0; (methotrexate)
 15475-56-6, 59-05-2, 7413-34-5
 CN (1) Bch 4556; Sti 571
 CO (1) Suire biochem (Canada)

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ACCESSION NUMBER: 2002227269 EMBASE

TITLE: Troxacitabine-based therapy of refractory
 leukemia.

AUTHOR: Giles F.J.

CORPORATE SOURCE: Dr. F.J. Giles, Section of Develop. Therapeutics, Univ. of
 TX M.D. Anderson Cancer Ctr, Department of Leukemia, 1515
 Holcombe Boulevard, Houston, TX 77030-4095, United States.
 fgiles@mdanderson.org

SOURCE: Expert Review of Anticancer Therapy, (2002) 2/3 (261-266).
 Refs: 38

ISSN: 1473-7140 CODEN: ERATBJ

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Unique among currently approved or in-development nucleoside analogs, **troxacitabine** (Troxatyl.RTM.) is an L-nucleoside with significant cytotoxic activity. Its stereochemistry and cellular transport characteristics render it insensitive to some tumor cell mechanisms of resistance to D-nucleosides, such as cytarabine and fludarabine. **Troxacitabine**'s dose-limiting toxicities were mucositis and hand-foot syndrome in patients with refractory leukemia. Three complete and one partial remissions were observed in 30 patients with refractory acute myeloid leukemia on a Phase I study. Significant activity in blastic phase of chronic myeloid leukemia was seen on a Phase II study. Combinations of **troxacitabine** with ara-C, topotecan and idarubicin are active in patients with refractory acute myeloid leukemia (AML). Phase II studies in patients with refractory lymphoproliferative diseases are ongoing. **Troxacitabine** merits further study in patients with hematological malignancies.

CT Medical Descriptors:

*acute granulocytic leukemia: DT, drug therapy

*acute granulocytic leukemia: TH, therapy

cytotoxicity

drug activity

stereochemistry

cell transport

sensitivity analysis

tumor cell

cell activity

drug response

mucosa inflammation: SI, side effect

hand foot syndrome: DT, drug therapy

hand foot syndrome: SI, side effect

cancer regression

lymphoproliferative disease: DT, drug therapy

hematologic disease

prostate cancer: DT, drug therapy

stem cell transplantation

rash: DT, drug therapy

rash: SI, side effect

drug blood level

fatigue: SI, side effect

gastrointestinal symptom: SI, side effect

bone marrow hypoplasia: SI, side effect

liver disease: SI, side effect

hyperbilirubinemia: SI, side effect

drug efficacy

human

clinical trial

controlled study

adult

article

Drug Descriptors:

*troxacitabine: AE, adverse drug reaction

*troxacitabine: CT, clinical trial

*troxacitabine: AN, drug analysis

*troxacitabine: CB, drug combination

*troxacitabine: CM, drug comparison
*troxacitabine: CR, drug concentration
*troxacitabine: DO, drug dose
*troxacitabine: DT, drug therapy
*troxacitabine: PK, pharmacokinetics
*troxacitabine: PD, pharmacology
*troxacitabine: IV, intravenous drug administration
cytarabine: AE, adverse drug reaction
cytarabine: CT, clinical trial
cytarabine: AN, drug analysis
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DO, drug dose
cytarabine: DT, drug therapy
cytarabine: PK, pharmacokinetics
cytarabine: PD, pharmacology
cytarabine: IV, intravenous drug administration
fludarabine: AN, drug analysis
fludarabine: CM, drug comparison
fludarabine: PK, pharmacokinetics
fludarabine: PD, pharmacology
topotecan: AE, adverse drug reaction
topotecan: CT, clinical trial
topotecan: AN, drug analysis
topotecan: CB, drug combination
topotecan: DO, drug dose
topotecan: DT, drug therapy
topotecan: PK, pharmacokinetics
topotecan: PD, pharmacology
topotecan: IV, intravenous drug administration
idarubicin: AE, adverse drug reaction
idarubicin: CT, clinical trial
idarubicin: AN, drug analysis
idarubicin: CB, drug combination
idarubicin: CM, drug comparison
idarubicin: DO, drug dose
idarubicin: DT, drug therapy
idarubicin: PK, pharmacokinetics
idarubicin: PD, pharmacology
idarubicin: IV, intravenous drug administration
5 aza 2' deoxycytidine: AN, drug analysis
5 aza 2' deoxycytidine: CM, drug comparison
5 aza 2' deoxycytidine: DV, drug development
5 aza 2' deoxycytidine: PK, pharmacokinetics
5 aza 2' deoxycytidine: PD, pharmacology
506 u78: AN, drug analysis
506 u78: CM, drug comparison
506 u78: DV, drug development
506 u78: PD, pharmacology
clofarabine: AN, drug analysis
clofarabine: CM, drug comparison
clofarabine: DV, drug development
clofarabine: PD, pharmacology
nucleoside derivative: AE, adverse drug reaction
nucleoside derivative: CT, clinical trial
nucleoside derivative: AN, drug analysis
nucleoside derivative: CM, drug comparison
nucleoside derivative: DV, drug development
nucleoside derivative: DT, drug therapy
nucleoside derivative: PK, pharmacokinetics

nucleoside derivative: PD, pharmacology
 lamivudine: PD, pharmacology
 deoxycytidine: AN, drug analysis
 deoxycytidine: CM, drug comparison
 deoxycytidine: PK, pharmacokinetics
 deoxycytidine: PD, pharmacology
 prednisone: DT, drug therapy
 prednisone: PD, pharmacology
 prednisone: PO, oral drug administration
 pyridoxine: DT, drug therapy
 pyridoxine: PD, pharmacology
 dimethyl sulfoxide: DT, drug therapy
 dimethyl sulfoxide: PD, pharmacology
 dimethyl sulfoxide: TP, topical drug administration
 imatinib: PD, pharmacology
 unclassified drug

RN (troxacitabine) 145918-75-8; (cytarabine) 147-94-4,
 69-74-9; (fludarabine) 21679-14-1; (topotecan) 119413-54-6, 123948-87-8;
 (idarubicin) 57852-57-0, 58957-92-9; (5 aza 2' deoxycytidine) 2353-33-5;
 (lamivudine) 134678-17-4, 134680-32-3; (deoxycytidine) 951-77-9;
 (prednisone) 53-03-2; (pyridoxine) 12001-77-3, 58-56-0, 65-23-6,
 8059-24-3; (dimethyl sulfoxide) 67-68-5; (imatinib) 152459-95-5,
 220127-57-1

CN (1) Troxatyl

CO (1) Shire (Canada)

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ACCESSION NUMBER: 2002367914 EMBASE

TITLE: Troxacitabine activity in extramedullary myeloid
 leukemia.

AUTHOR: Alvarado Y.Yesid; Kantarjian H.M.; Cortes J.E.; Apostolidou
 E.; Bivins C.; Giles F.J.

CORPORATE SOURCE: F.J. Giles, Department of Leukemia, M.D. Anderson Cancer
 Center, The University of Texas, 1400 Holcombe Boulevard,
 Houston, TX 77030, United States. frankgiles@aol.com

SOURCE: Hematology, (2002) 7/3 (179-185)..

Refs: 36

ISSN: 1024-5340 CODEN: HMATFL

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
 025 Hematology
 037 Drug Literature Index
 038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Troxacitabine is a novel L-enantiomer nucleoside analog with
 unique properties in terms of its structure, pharmacokinetics,
 intracellular transport, and susceptibility to mechanisms of resistance.
 Troxacitabine has significant activity in patients with refractory
 myeloid leukemias, both as a single agent and when combined with standard
 anti-leukemia agents. In a cohort of 170 patients with refractory myeloid
 leukemia treated with troxacitabine-based regimens on Phase 1 or
 2 studies, 10 (6%) had biopsy-proven extramedullary disease, either with
 or without bone marrow involvement. Six of these patients who received
 single-agent troxacitabine, 4 received a combination of
 troxacitabine and cytarabine. Complete response and disappearance
 of all extramedullary lesions were observed in 6 (60%) of these 10
 patients. Two of the 6 responding patients relapsed within 3 months, 2

patients had remissions of 8 and 9 months duration, respectively, 1 patient is in on-going remission at 3, and 1 patient is lost to follow-up. Troxacitabine-based therapy had significant antileukemic activity in extramedullary myeloid leukemias and warrants further investigation in this clinical situation.

CT Medical Descriptors:

- *myeloid leukemia: DI, diagnosis
- *myeloid leukemia: DR, drug resistance
- *myeloid leukemia: DT, drug therapy
- *myeloid leukemia: RT, radiotherapy
- *myeloid leukemia: TH, therapy

enantiomer

drug structure

drug transport

cohort analysis

biopsy

bone marrow

drug response

cancer recurrence

leukemia remission

disease duration

follow up

allogenic bone marrow transplantation

drug half life

treatment failure

mucosa inflammation: SI, side effect

hand foot syndrome: SI, side effect

rash: SI, side effect

human

male

female

major clinical study

clinical trial

phase 1 clinical trial

phase 2 clinical trial

controlled study

human tissue

aged

adult

article

priority journal

Drug Descriptors:

- *troxacitabine: AE, adverse drug reaction

- *troxacitabine: CT, clinical trial

- *troxacitabine: AN, drug analysis

- *troxacitabine: CB, drug combination

- *troxacitabine: CM, drug comparison

- *troxacitabine: DT, drug therapy

- *troxacitabine: PK, pharmacokinetics

- *troxacitabine: PD, pharmacology

- *troxacitabine: IV, intravenous drug administration

nucleoside analog: AE, adverse drug reaction

nucleoside analog: CT, clinical trial

nucleoside analog: AN, drug analysis

nucleoside analog: CB, drug combination

nucleoside analog: CM, drug comparison

nucleoside analog: DT, drug therapy

nucleoside analog: PK, pharmacokinetics

nucleoside analog: PD, pharmacology

nucleoside analog: IV, intravenous drug administration

antileukemic agent: AE, adverse drug reaction
 antileukemic agent: CT, clinical trial
 antileukemic agent: AN, drug analysis
 antileukemic agent: CB, drug combination
 antileukemic agent: CM, drug comparison
 antileukemic agent: DT, drug therapy
 antileukemic agent: PK, pharmacokinetics
 antileukemic agent: PD, pharmacology
 antileukemic agent: TL, intrathecal drug administration
 antileukemic agent: IV, intravenous drug administration
 cytarabine: AN, drug analysis
 cytarabine: CB, drug combination
 cytarabine: CM, drug comparison
 cytarabine: DT, drug therapy
 cytarabine: TL, intrathecal drug administration
 cytarabine: IV, intravenous drug administration
 idarubicin: CB, drug combination
 idarubicin: DT, drug therapy
 idarubicin: IV, intravenous drug administration
 topotecan: CB, drug combination
 topotecan: DT, drug therapy
 topotecan: IV, intravenous drug administration
 hydroxyurea: CB, drug combination
 hydroxyurea: DT, drug therapy
 interferon: CB, drug combination
 interferon: DT, drug therapy
 imatinib: CB, drug combination
 imatinib: DT, drug therapy
 busulfan: CB, drug combination
 busulfan: DT, drug therapy
 cyclophosphamide: CB, drug combination
 cyclophosphamide: DT, drug therapy
 fludarabine: AN, drug analysis
 fludarabine: CB, drug combination
 fludarabine: DT, drug therapy
 melphalan: CB, drug combination
 melphalan: DT, drug therapy
 5 aza 2' deoxycytidine: CB, drug combination
 5 aza 2' deoxycytidine: DT, drug therapy
 homoharringtonine: CB, drug combination
 homoharringtonine: DT, drug therapy
 monoclonal antibody: CB, drug combination
 monoclonal antibody: DT, drug therapy
 arsenic trioxide: CB, drug combination
 arsenic trioxide: DT, drug therapy
 methotrexate: CB, drug combination
 methotrexate: DT, drug therapy
 gemcitabine: AN, drug analysis

RN (troxacitabine) 145918-75-8; (cytarabine) 147-94-4,
 69-74-9; (idarubicin) 57852-57-0, 58957-92-9; (topotecan) 119413-54-6,
 123948-87-8; (hydroxyurea) 127-07-1; (imatinib) 152459-95-5,
 220127-57-1; (busulfan) 55-98-1; (cyclophosphamide) 50-18-0;
 (fludarabine) 21679-14-1; (melphalan) 148-82-3; (5 aza 2' deoxycytidine)
 2353-33-5; (homoharringtonine) 26833-87-4; (arsenic trioxide) 1303-24-8,
 1327-53-3, 13464-58-9, 15502-74-6; (methotrexate) 15475-56-6, 59-05-2,
 7413-34-5; (gemcitabine) 103882-84-4
 CN Gleevec; Sti 571
 CO Shire (Canada)

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on STN

ACCESSION NUMBER: 2002369569 EMBASE
 TITLE: STI-571 in chronic myelogenous
 leukaemia.
 AUTHOR: Tsao A.S.; Kantarjian H.; Talpaz M.
 CORPORATE SOURCE: M. Talpaz, Department of Bioimmunotherapy, MD Anderson
 Cancer Center, Box 422, 1515 Holcombe Blvd., Houston, TX
 77030, United States. mtalpaz@mdanderson.org
 SOURCE: British Journal of Haematology, (2002) 119/1 (15-24).
 Refs: 72
 ISSN: 0007-1048 CODEN: BJHEAL
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 016 Cancer
 025 Hematology
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 CT Medical Descriptors:
 *chronic myeloid leukemia: DT, drug therapy
 *chronic myeloid leukemia: SI, side effect
 *chronic myeloid leukemia: TH, therapy
 clinical feature
 disease course
 survival time
 pathogenesis
 cancer radiotherapy
 cancer chemotherapy
 cancer survival
 protein phosphorylation
 antineoplastic activity
 drug absorption
 drug half life
 cancer regression
 drug efficacy
 drug mechanism
 apoptosis
 cancer cell culture
 point mutation
 side effect: SI, side effect
 nausea: SI, side effect
 muscle cramp: SI, side effect
 arthralgia: SI, side effect
 myalgia: SI, side effect
 edema: SI, side effect
 rash: SI, side effect
 bone marrow suppression: SI, side effect
 diarrhea: SI, side effect
 liver toxicity: SI, side effect
 neutropenia: SI, side effect
 thrombocytopenia: SI, side effect
 allogenic bone marrow transplantation
 human
 nonhuman
 clinical trial
 article
 priority journal
 Drug Descriptors:
 *imatinib: AE, adverse drug reaction

*imatinib: CT, clinical trial
 *imatinib: CB, drug combination
 *imatinib: CM, drug comparison
 *imatinib: DO, drug dose
 *imatinib: DT, drug therapy
 *imatinib: PK, pharmacokinetics
 *imatinib: PD, pharmacology
 *imatinib: PO, oral drug administration
 busulfan: AE, adverse drug reaction
 busulfan: CB, drug combination
 busulfan: DT, drug therapy
 busulfan: PD, pharmacology
 hydroxyurea: DT, drug therapy
 hydroxyurea: PD, pharmacology
 cyclophosphamide: CB, drug combination
 cyclophosphamide: DT, drug therapy
 cyclophosphamide: PD, pharmacology
 alpha interferon: AE, adverse drug reaction
 alpha interferon: CT, clinical trial
 alpha interferon: CB, drug combination
 alpha interferon: CM, drug comparison
 alpha interferon: DT, drug therapy
 alpha interferon: PD, pharmacology
 cytarabine: CT, clinical trial
 cytarabine: CB, drug combination
 cytarabine: DT, drug therapy
 cytarabine: PD, pharmacology
 BCR ABL protein: EC, endogenous compound
 homoharringtonine: DT, drug therapy
 5 aza 2' deoxycytidine: DT, drug therapy

troxacitabine: DT, drug therapy

orosomucoid: EC, endogenous compound

verapamil: DT, drug therapy

verapamil: PD, pharmacology

leptomycin B: CB, drug combination

leptomycin B: DT, drug therapy

leptomycin B: PD, pharmacology

RN (imatinib) 152459-95-5, 220127-57-1; (busulfan) 55-98-1;
 (hydroxyurea) 127-07-1; (cyclophosphamide) 50-18-0; (cytarabine) 147-94-4,
 69-74-9; (homoharringtonine) 26833-87-4; (5 aza 2' deoxycytidine)
 2353-33-5; (**troxacitabine**) 145918-75-8; (orosomucoid)
 79921-18-9; (verapamil) 152-11-4, 52-53-9; (leptomycin B) 87081-35-4
 CN **Sti 571; Glivec; Cgp 57148b; Gleevec**

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on STN

ACCESSION NUMBER: 2002320865 EMBASE

TITLE: Chronic myeloid leukemia: Current therapies and the potential role of farnesyltransferase inhibitors.

AUTHOR: Keating A.

CORPORATE SOURCE: Dr. A. Keating, Princess Margaret Hospital, 610 University Ave, Toronto, Ont. M5G 2M9, Canada

SOURCE: Seminars in Hematology, (2002) 39/3 SUPPL. 2 (11-17).
Refs: 59

ISSN: 0037-1963 CODEN: SEHEA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The treatment of patients with chronic myeloid leukemia (CML) is evolving rapidly. With conventional chemotherapy the clinical course is characterized by a chronic phase (median duration, 4 to 5 years), followed by an accelerated phase with transition to a terminal blast crisis. Treatment with busulfan or hydroxyurea does not alter the natural history. Interferon alfa (IFN- α) prolongs life expectancy by approximately 20 months but is associated with significant toxicity. Evidence indicates that bone marrow transplantation from a related human leukocyte antigen (HLA)-identical donor can be curative in younger patients. However, transplantation is available to only a minority of patients and entails severe toxicity and transplant-related mortality. Dramatic advances in the understanding of the molecular pathophysiology of CML have led to a new era of targeted therapy. The specific tyrosine kinase inhibitor **imatinib mesylate** demonstrates a high level of efficacy in CML with acceptable toxicity. Farnesyltransferase inhibitors (FTIs) are another important class of targeted agents with the potential to act at multiple sites within dysregulated signal transduction networks. ZARNESTRA[®] (formerly R115777, Ortho Biotech Oncology, Raritan, NJ), an oral FTI, has shown activity and is well tolerated in both chronic- and accelerated-phase patients. With their mechanistic specificity, the new modalities offer the promise of increased antileukemic activity and an improved therapeutic index. Copyright 2002, Elsevier Science (USA). All rights reserved.

CT Medical Descriptors:

*chronic myeloid leukemia: DT, drug therapy

*chronic myeloid leukemia: TH, therapy
disease course

blast cell crisis

life expectancy

cancer survival

bone marrow transplantation

drug efficacy

drug tolerability

treatment outcome

bone marrow suppression: SI, side effect

diarrhea: SI, side effect

nausea: SI, side effect

vomiting: SI, side effect

headache: SI, side effect

fatigue: SI, side effect

tachycardia: SI, side effect

human

clinical trial

article

priority journal

Drug Descriptors:

*protein farnesyltransferase inhibitor: CT, clinical trial

*protein farnesyltransferase inhibitor: DT, drug therapy

*protein farnesyltransferase inhibitor: PO, oral drug administration

*r 115777: CT, clinical trial

*r 115777: DT, drug therapy

*r 115777: PO, oral drug administration

busulfan: DT, drug therapy

hydroxyurea: DT, drug therapy

recombinant alpha2b interferon: AE, adverse drug reaction

recombinant alpha2b interferon: CT, clinical trial

recombinant alpha2b interferon: DT, drug therapy

protein tyrosine kinase inhibitor: DT, drug therapy

imatinib: AE, adverse drug reaction

imatinib: DT, drug therapy

cytarabine: DT, drug therapy

homoharringtonine: AE, adverse drug reaction

homoharringtonine: DV, drug development

homoharringtonine: DT, drug therapy

5 aza 2' deoxycytidine: DT, drug therapy

troxacitabine: CT, clinical trial

troxacitabine: DT, drug therapy

3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2

thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial

3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2

thienylsulfonyl) 1h 1,4 benzodiazepine: DT, drug therapy

3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2

thienylsulfonyl) 1h 1,4 benzodiazepine: IV, intravenous drug

administration

4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide: CT, clinical trial

4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide: DT, drug therapy

4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide: PO, oral drug administration

zarnestra

- RN (busulfan) 55-98-1; (hydroxyurea) 127-07-1; (recombinant alpha2b interferon) 98530-12-2; (imatinib) 152459-95-5, 220127-57-1; (cytarabine) 147-94-4, 69-74-9; (homoharringtonine) 26833-87-4; (5 aza 2' deoxycytidine) 2353-33-5; (**troxacitabine**) 145918-75-8; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide) 193275-84-2
- CN (1) Zarnestra; (2) Myleran; (3) Hydrea; (4) Intron A; (5) Cytosar u; (6) **Gleevec**; (7) Decitabine; (8) **Bch 4556**; (9) Bms 214662; (10) Sch 66336
- CO (1) Ortho (United States); (2) Glaxo SmithKline (United States); (4) Schering Corporation (United States); (5) Bedford (United States); (6) Novartis (United States); (7) Supergen (United States); (8) Biochem Corporation (Canada); (9) Bristol Myers Squibb (United States); (10) Schering Plough (United States)

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ACCESSION NUMBER: 2002320864 EMBASE

TITLE: Treatment of acute myeloid leukemia: State-of-the-art and future directions.

AUTHOR: Stone R.M.

CORPORATE SOURCE: Dr. R.M. Stone, Dana-Farber Cancer Institute, 44 Binney St, Boston, MA 02115, United States

SOURCE: Seminars in Hematology, (2002) 39/3 SUPPL. 2 (4-10).
Refs: 66

ISSN: 0037-1963 CODEN: SEHEA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer

025 Hematology

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Despite major recent advances in the understanding of the molecular biology of the disease, the treatment of acute myeloid leukemia (AML) in adults remains challenging. For the 75% of AML patients older than 60 years, currently available treatments produce significant toxicity with poor overall response rates and survival. In younger patients, standard regimens using cytarabine and an anthracycline for induction followed by some form of intensive postremission therapy can produce response rates of 70% with 5-year relapse-free survival rates of 25% to 40%. Chromosomal analyses define three prognostic categories with favorable, intermediate, and unfavorable risk. In older adults, AML appears to be an intrinsically resistant disorder of proximal pluripotent hematopoietic stem cells. A variety of targeted therapies currently in development include modulators of MDR1-mediated drug resistance, immunotherapeutics, angiogenesis inhibitors, proapoptotic antisense oligonucleotides, and specific small molecule inhibitors of **tyrosine kinase** and farnesyltransferase. For example, oral farnesyltransferase inhibitors have demonstrated activity and tolerability in patients with refractory AML and are now in phase II testing. Such targeted therapeutics offer the promise of novel antileukemic activity combined with an improved therapeutic index. Copyright 2002, Elsevier Science (USA). All rights reserved.

CT Medical Descriptors:

*acute granulocytic leukemia: DT, drug therapy

treatment outcome

cancer survival

age

cancer regression

cancer recurrence

drug response

chromosome analysis

prognosis

hematopoietic stem cell

cancer combination chemotherapy

immunotherapy

multidrug resistance

stomatitis: SI, side effect

bone marrow suppression: SI, side effect

infection: SI, side effect

bleeding: SI, side effect

mucosa inflammation: SI, side effect

nausea: SI, side effect

vomiting: SI, side effect

cardiotoxicity: SI, side effect

human

clinical trial

article

priority journal

Drug Descriptors:

cytarabine: CT, clinical trial

cytarabine: CB, drug combination

cytarabine: DT, drug therapy

anthracycline: CB, drug combination

anthracycline: DT, drug therapy

angiogenesis inhibitor: DV, drug development

angiogenesis inhibitor: DT, drug therapy

antisense oligonucleotide: DV, drug development

antisense oligonucleotide: DT, drug therapy

protein tyrosine kinase inhibitor: DV, drug development

protein tyrosine kinase inhibitor: DT, drug therapy
 protein farnesyltransferase inhibitor: CT, clinical trial
 protein farnesyltransferase inhibitor: DV, drug development
 protein farnesyltransferase inhibitor: DT, drug therapy
 protein farnesyltransferase inhibitor: PD, pharmacology
 protein farnesyltransferase inhibitor: PO, oral drug administration
 antineoplastic agent: AE, adverse drug reaction
 antineoplastic agent: DT, drug therapy
 cladribine: DT, drug therapy
 granulocyte colony stimulating factor: CT, clinical trial
 granulocyte colony stimulating factor: DT, drug therapy
 cyclophosphamide: CB, drug combination
 cyclophosphamide: DT, drug therapy
 etoposide: CT, clinical trial
 etoposide: CB, drug combination
 etoposide: DT, drug therapy
 diaziquone: CB, drug combination
 diaziquone: DT, drug therapy
 mitoxantrone: CB, drug combination
 mitoxantrone: DT, drug therapy
 topotecan: CB, drug combination
 topotecan: DT, drug therapy
 troxacitabine: AE, adverse drug reaction
 troxacitabine: CT, clinical trial
 troxacitabine: DT, drug therapy
 idarubicin: CB, drug combination
 idarubicin: DT, drug therapy
 cyclosporin: CT, clinical trial
 cyclosporin: CB, drug combination
 cyclosporin: DT, drug therapy
 valspodar: CT, clinical trial
 valspodar: CB, drug combination
 valspodar: DT, drug therapy
 daunorubicin: CT, clinical trial
 daunorubicin: CB, drug combination
 daunorubicin: DT, drug therapy
 granulocyte macrophage colony stimulating factor: CT, clinical trial
 granulocyte macrophage colony stimulating factor: DT, drug therapy
 gemtuzumab ozogamicin: DT, drug therapy
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
 thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
 thienylsulfonyl) 1h 1,4 benzodiazepine: DT, drug therapy
 3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
 thienylsulfonyl) 1h 1,4 benzodiazepine: IV, intravenous drug
 administration
 zarnestra

RN (cytarabine) 147-94-4, 69-74-9; (cladribine) 4291-63-8; (cyclophosphamide)
 50-18-0; (etoposide) 33419-42-0; (diaziquone) 57998-68-2; (mitoxantrone)
 65271-80-9, 70476-82-3; (topotecan) 119413-54-6, 123948-87-8; (
 troxacitabine) 145918-75-8; (idarubicin) 57852-57-0,
 58957-92-9; (cyclosporin) 79217-60-0; (valspodar) 121584-18-7;
 (daunorubicin) 12707-28-7, 20830-81-3, 23541-50-6; (3 benzyl 7 cyano
 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4
 benzodiazepine) 195981-08-9, 195987-41-8
 CN (1) Bms 214662; Zarnestra; Psc 833
 CO (1) Schering Plough (United States)

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 on STN

ACCESSION NUMBER: 2002320863 EMBASE
TITLE: Assessing the future landscape in myeloid malignancies:
Evolving insights on farnesyltransferase inhibitors:
Introduction.
AUTHOR: Rosenblatt J.D.; Rowe J.M.
CORPORATE SOURCE: Dr. J.D. Rosenblatt, Hematology-Oncology Division,
University of Miami, Sylvester Compreh. Cancer Center, 1475
NW 12th Ave, Miami, FL 33136, United States
SOURCE: Seminars in Hematology, (2002) 39/3 SUPPL. 2 (1-3).
Refs: 1
ISSN: 0037-1963 CODEN: SEHEA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
LANGUAGE: English
CT Medical Descriptors:
*leukemia: DT, drug therapy
acute granulocytic leukemia: DT, drug therapy
chronic myeloid leukemia: DT, drug therapy
myelodysplastic syndrome: DT, drug therapy
treatment planning
treatment outcome
human
clinical trial
editorial
priority journal
Drug Descriptors:
protein farnesyltransferase inhibitor: CT, clinical trial
protein farnesyltransferase inhibitor: DT, drug therapy
retinoic acid: DT, drug therapy
imatinib: DT, drug therapy
r 115777: CT, clinical trial
r 115777: DT, drug therapy
topotecan: DT, drug therapy
troxycitabine: DT, drug therapy
valspodar: DT, drug therapy
1 [4 (11,11 difluorodibenzo[b,e]bicyclo[5.1.0]oct 5 yl) 1 piperazinyl] 3
(5 quinolinyl) 2 propanol: DT, drug therapy
g 3139: DT, drug therapy
4 [2 [4 (3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2
b]pyridin 11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide: DT,
drug therapy
zarnestra
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
thienylsulfonyl) 1h 1,4 benzodiazepine
RN (retinoic acid) 302-79-4; (imatinib) 152459-95-5, 220127-57-1;
(topotecan) 119413-54-6, 123948-87-8; (troxycitabine)
145918-75-8; (valspodar) 121584-18-7; (1 [4 (11,11
difluorodibenzo[b,e]bicyclo[5.1.0]oct 5 yl) 1 piperazinyl] 3 (5
quinolinyl) 2 propanol) 167465-36-3; (g 3139) 190977-41-4; (4 [2 [4
(3,10 dibromo 8 chloro 6,11 dihydro 5h benzo[5,6]cyclohepta[1,2 b]pyridin
11 yl) 1 piperidinyl] 2 oxoethyl] 1 piperidinecarboxamide) 193275-84-2; (3
benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2
thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8
CN (1) Gleevec; (2) Zarnestra; (3) Hycamtin; (4) Bch 4556
; (5) Sch 66336; (6) Bms 214662; Psc 833; Ly 335979; G 3139
CO (1) Novartis (United States); (2) Ortho (United States); (3) Glaxo
SmithKline (United States); (4) Biochem Pharma (Canada); (5) Schering

Plough (United States); (6) Bristol Myers Squibb (United States)

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ACCESSION NUMBER: 2001169089 EMBASE
TITLE: Latest advances from basic and clinical research in
hematology.
AUTHOR: Diaz-Ricart M.
CORPORATE SOURCE: Dr. M. Diaz-Ricart, Hemotherapy Dept. of the Hosp. Clin.,
IDIBAPS, Villarroel 170, 08036 Barcelona, Spain
SOURCE: Drug News and Perspectives, (2001) 14/1 (50-53).
ISSN: 0214-0934 CODEN: DNPEED
COUNTRY: Spain
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB New treatments in hematological malignancies were a focal point of
sessions and presentations at the 42nd Annual Meeting of the American
Society of Hematology, held December 1-5, 2000, in San Francisco,
California, U.S.A. The meeting also provided discussion on pathogen
inactivation in blood banking, stem cell transplantation in leukemia as
well as nonmalignant diseases, the reparative potential of stem cells, a
new oral antithrombotic therapy and a new class of highly selective factor
Xa inhibitors. .COPYRGT. 2001 Prous Science.

CT Medical Descriptors:
*leukemia: DT, drug therapy
stem cell transplantation
drug safety
hematologic disease
stem cell
blood bank
antineoplastic activity
conference paper
Drug Descriptors:
anticoagulant agent: PO, oral drug administration
antineoplastic agent: DT, drug therapy
inactive
s 59
 glivec
 troxatyl
myolotarg
h 376 95

CN (1) Inactine; (2) S 59; (3) Glivec; (4) Troxatyl; (5)
Myolotarg; (6) H 376 95

CO (1) Vitek; (2) Baxter; (3) Novartis; (4) Biochem Corporation; (5) Wyeth;
(6) Astra Zeneca

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ACCESSION NUMBER: 1999376440 EMBASE
TITLE: Novel anti-cancer agents in development: Exciting prospects
and new challenges.
AUTHOR: Seymour L.
CORPORATE SOURCE: L. Seymour, National Cancer Institute of Canada, Clinical
Trials Group, Queens University, 18 Barrie Street,
Kingston, Ont. K7L 3N6, Canada
SOURCE: Cancer Treatment Reviews, (1999) 25/5 (301-312).

Refs: 105
ISSN: 0305-7372 CODEN: CTREDJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A large number of cancer chemotherapeutic agents are in development, many already undergoing clinical testing. A number of these compounds were designed either to modulate or inhibit molecular targets which have been identified as being critical to the development or control of cancer. Targets for inhibition include matrix metalloproteinases, mediators of signal transduction (**tyrosine kinases**, cyclin dependent kinases and other kinases such as protein kinase C and A) as well as ras expression and prenylation. Classes of potential inhibitory compounds include small molecules, humanized monoclonal antibodies or antisense oligonucleotides. Many of these compounds are relatively well advanced in development. Proof of principle has already been demonstrated in some instances and at least one such compound has been approved for use. Although these new compounds offer exciting opportunities, many bring with them real challenges in terms of the selection of appropriate trial design and surrogate end-points.

CT Medical Descriptors:

drug design
drug targeting
cancer control
signal transduction
oncogene ras
gene expression
prenylation
methodology
cancer: DT, drug therapy
pancreas cancer: DT, drug therapy
lung non small cell cancer: DT, drug therapy
lung small cell cancer: DT, drug therapy
prostate cancer: DT, drug therapy
ovary cancer: DT, drug therapy
musculoskeletal disease: SI, side effect
rash: SI, side effect
anemia: SI, side effect
thrombocytopenia: SI, side effect
gastrointestinal symptom: SI, side effect
liver toxicity: SI, side effect
drug hypersensitivity: SI, side effect
hypotension: SI, side effect
cardiotoxicity: SI, side effect
fatigue: SI, side effect
headache: SI, side effect
fever: SI, side effect
human
clinical trial
review

Drug Descriptors:

*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: DT, drug therapy
matrix metalloproteinase: EC, endogenous compound

cyclin dependent kinase: EC, endogenous compound
protein tyrosine kinase: EC, endogenous compound
protein kinase c: EC, endogenous compound
cyclic AMP dependent protein kinase: EC, endogenous compound
monoclonal antibody: DV, drug development
antisense oligonucleotide
2' deoxy 3' oxacytidine: CT, clinical trial
2' deoxy 3' oxacytidine: DT, drug therapy
4 [4,4 (chlorophenyl)phenyl] 4 oxo (phenylthiomethyl)butanoic acid: CT,
clinical trial
4 [4,4 (chlorophenyl)phenyl] 4 oxo (phenylthiomethyl)butanoic acid: DT,
drug therapy
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
fluorouracil: CT, clinical trial
fluorouracil: CB, drug combination
fluorouracil: DT, drug therapy
aplidine: CT, clinical trial
aplidine: DT, drug therapy
zd 1839: AE, adverse drug reaction
zd 1839: CT, clinical trial
zd 1839: DT, drug therapy
bryostatin: AE, adverse drug reaction
bryostatin: CT, clinical trial
bryostatin: DT, drug therapy
isis 3521: AE, adverse drug reaction
isis 3521: CT, clinical trial
isis 3521: DT, drug therapy
cgp 69846a: CT, clinical trial
cgp 69846a: DT, drug therapy
flavopiridol: CT, clinical trial
flavopiridol: DT, drug therapy
sch 66366: CT, clinical trial
sch 66366: DT, drug therapy
batimastat: CT, clinical trial
batimastat: DT, drug therapy
marimastat: AE, adverse drug reaction
marimastat: CT, clinical trial
marimastat: DT, drug therapy
ag 3340: AE, adverse drug reaction
ag 3340: CT, clinical trial
ag 3340: DT, drug therapy
cgs 27023a: AE, adverse drug reaction
cgs 27023a: CT, clinical trial
cgs 27023a: DT, drug therapy
bms 275291: CT, clinical trial
bms 275291: DT, drug therapy
col 3: CT, clinical trial
col 3: DT, drug therapy
a 177430: CT, clinical trial
a 177430: DT, drug therapy
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: CT, clinical trial
4 (3 bromoanilino) 6,7 dimethoxyquinazoline: DT, drug therapy
unindexed drug
[6,7 bis(2 methoxy ethoxy)quinazoline 4 yl](3 ethynylphenyl)amine: AE,
adverse drug reaction
[6,7 bis(2 methoxy ethoxy)quinazoline 4 yl](3 ethynylphenyl)amine: CT,
clinical trial
[6,7 bis(2 methoxy ethoxy)quinazoline 4 yl](3 ethynylphenyl)amine: DT,

drug therapy
 cgp 59326: CT, clinical trial
 cgp 59326: DT, drug therapy
 epidermal growth factor receptor antibody
 RN (cyclin dependent kinase) 150428-23-2; (protein tyrosine
 kinase) 80449-02-1; (protein kinase c) 141436-78-4; (doxorubicin)
 23214-92-8, 25316-40-9; (fluorouracil) 51-21-8; (isis 3521) 151879-73-1;
 (cgp 69846a) 177075-18-2; (flavopiridol) 146426-40-6; (batimastat)
 130370-60-4, 130464-84-5; (marimastat) 154039-60-8; (ag 3340) 195008-93-6;
 (cgs 27023a) 169799-04-6
 CN (1) Bb 94; (2) Bb 2516; (3) Ag 3340; (4) Cgs 27023a; (5) Cgp 59326; (6)
 Bay 12 9566; (7) Bms 275291; (8) Col 3; (9) A 177430; (10) Zd 1839; (11)
 Pd 153035; (12) Cp 358774; (13) C 225; (14) Isis 3521; (15) Isis 5132;
 (16) Sch 66366; **Bch 4556**
 CO (2) British Biotechnology; (3) Agouron; (5) Novartis; (6) Bayer; (7)
 Bristol Myers Squibb; (8) Collagenex; (9) Abbott; (10) Astra; (11) Parke
 Davis; (12) Pfizer; (13) Imclone; (15) Isis; (16) Schering Plough;
 Abgenix; Genentech; Sugen; Hybridon; Kyowa Hakko Kogyo; Hoechst Marion
 Roussel; Medarex; Merck; Janssen

L89 ANSWER 38 OF 54 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
 STN

ACCESSION NUMBER: 2002:152475 BIOSIS
 DOCUMENT NUMBER: PREV200200152475
 TITLE: Phase II study of TroxatylTM in patients with chronic
 myeloid leukemia in blastic phase (CML-BP).
 AUTHOR(S): Giles, Francis [Reprint author]; Feldman, Eric; Cortes,
 Jorge [Reprint author]; Faderl, Stefan [Reprint author];
 Larson, Richard; Mamus, Steven; Thomas, Deborah [Reprint
 author]; Garcia-Manero, Guillermo [Reprint author];
 O'Brien, Susan [Reprint author]; Beran, Milsolav [Reprint
 author]; Talpaz, Moshe [Reprint author]; Kantarjian, Hagop
 [Reprint author]
 CORPORATE SOURCE: UT MD Anderson Cancer Center, Houston, TX, USA
 SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp.
 258b. print.
 Meeting Info.: 43rd Annual Meeting of the American Society
 of Hematology, Part 2. Orlando, Florida, USA. December
 07-11, 2001. American Society of Hematology.
 CODEN: BLOOAW. ISSN: 0006-4971.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 21 Feb 2002
 Last Updated on STN: 26 Feb 2002

ED Entered STN: 21 Feb 2002

Last Updated on STN: 26 Feb 2002

AB **Troxatyl** triphosphate (converted by the intracellular
 phosphorylation of **Troxatyl**) is a potent inhibitor and chain
 terminator for human cellular DNA polymerases and was a unique pattern of
 cellular uptake and metabolism. On a Phase I study, **Troxatyl**
 had significant antileukemia activity in patients with refractory disease.
 (Giles et al, JCO: 19:762:2001). The recommended single agent dose was
 defined as 8 mg/m²/day daily for 5 days. On a subsequent Phase II study,
 6 patients with CML-BP of 16 evaluable (37%) achieved a return to chronic
 phase disease. (Giles et al, JCO: In press). Three of the 6 responding
 patients received **Troxatyl** as first therapy for CML-BP; one
 patient had failed STI571 as prior sole therapy for CML-BP. A multicenter
 Phase II study of **Troxatyl** 8 mg/m²/day daily for 5 days for
 patients with CML-BP who have received no prior chemotherapy for CML-BP is

being conducted. Patients who have received **Gleevec** therapy as sole prior therapy for CML-BP are also eligible. Twenty-six patients, 17 male, 26 performance score ≥ 2 , median age 54 years (range 31-84) have been entered on study to date, 13 (50%) patients received **Troxatyl** as first therapy for CML-BP, 13 (50%) had failed prior **Gleevec** therapy for CML-BP. Response definitions are as follows: Complete hematologic response (CHR) requires normalization of peripheral counts and differentials with $\leq 5\%$ marrow blasts for at least 4 weeks. Hematologic improvement (HI) is as with CHR but with persistence of thrombocytopenia less than $100 \times 10^9/L$ and few immature peripheral cells. A partial hematologic response (PHR) is as per CHR, but allows persistence of, though $\geq 50\%$ reduction of, palpable splenomegaly and thrombocytosis (platelets $> 450 \times 10^9/L$), or the presence of few immature peripheral cells. Back to second chronic phase (BCP) requires disappearance of BP features and return to chronic phase CML features, i.e., peripheral blasts $< 15\%$, peripheral blasts+promyelocytes $< 30\%$, peripheral basophils $< 20\%$, and platelets $> 100 \times 10^9/L$. In patients with extramedullary disease (EMD), complete response (CR) requires CHR plus disappearance of all EMD. PR in patients with EMD require at least a 50% reduction in all EMD. Twenty-one patients who have received a total of 40 cycles (range 1 to 4) of **Troxatyl** therapy are currently evaluable for response - 1 PR, 1 HI, 1 BCP, and 1 CR in a patient with EMD have been recorded to date. Four patients died during cycle 1 of therapy - one with a CVA, 3 with sepsis/progressive disease. Extramedullary grade 3 or 4 attributable adverse events in the first cycle of therapy included skin rash (3), hyperbilirubinemia (3), hand foot syndrome (1), colitis (1). One patient developed Sweets Syndrome during 1st cycle of therapy - this subsequently completely resolved. Median survival in the study cohort is 9 months with 33% of patients alive at 1 year. **Troxatyl** has significant activity in patients with CML-BP. Accrual continues on this study.

- CC General biology - Symposia, transactions and proceedings . 00520
 Cytology - Animal 02506
 Cytology - Human 02508
 Pathology - Therapy 12512
 Metabolism - Metabolic disorders 13020
 Digestive system - Pathology 14006
 Blood - Blood and lymph studies 15002
 Blood - Blood cell studies 15004
 Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
 Integumentary system - Pathology 18506
 Pharmacology - General 22002
 Pharmacology - Clinical pharmacology 22005
 Toxicology - General and methods 22501
 Toxicology - Pharmacology 22504
 Neoplasms - Immunology 24003
 Neoplasms - Pathology, clinical aspects and systemic effects 24004
 Neoplasms - Therapeutic agents and therapy 24008
 Neoplasms - Blood and reticuloendothelial neoplasms 24010
 Gerontology - 24500
 Immunology - General and methods 34502
 Immunology - Immunopathology, tissue immunology 34508
 Medical and clinical microbiology - General and methods 36001
- IT Major Concepts
 Clinical Immunology (Human Medicine, Medical Sciences); Hematology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Pharmacology
- IT Parts, Structures, & Systems of Organisms
 basophil: blood and lymphatics, immune system; marrow blast: blood and lymphatics; platelet: blood and lymphatics; spleen: blood and

lymphatics, immune system

IT Diseases
chronic myeloid leukemia in blastic phase: blood and lymphatic disease,
neoplastic disease, drug therapy

IT Diseases
colitis: digestive system disease, toxicity
Colitis (MeSH)

IT Diseases
extramedullary disease: disease-miscellaneous

IT Diseases
hand foot syndrome: toxicity

IT Diseases
hyperbilirubinemia: metabolic disease, toxicity
Hyperbilirubinemia (MeSH)

IT Diseases
sepsis: infectious disease
Sepsis (MeSH)

IT Diseases
splenomegaly: blood and lymphatic disease
Splenomegaly (MeSH)

IT Diseases
sweet syndrome: integumentary system disease, toxicity

IT Diseases
thrombocytopenia: blood and lymphatic disease, drug-induced
Thrombocytopenia (MeSH)

IT Diseases
thrombocytosis: blood and lymphatic disease, drug-induced
Thrombocytosis (MeSH)

IT Chemicals & Biochemicals
Troxatyl: antineoplastic-drug, Phase II clinical trial

IT Miscellaneous Descriptors
complete hematologic response; partial hematologic response; Meeting
Abstract

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: adult, aged, aged/80 and over, female, male, middle age, patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L89 ANSWER 39 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-34978 DRUGU T
TITLE: Novel therapies for myeloplastic syndromes.
AUTHOR: Faderl S; Kantarjian H M
CORPORATE SOURCE: Univ.Texas-Syst.
LOCATION: Houston, Tex., USA
SOURCE: Cancer (101, No. 2, 226-41, 2004) 4 Fig. 6 Tab. 132 Ref.
CODEN: CANCAR ISSN: 0008-543X
AVAIL. OF DOC.: Department of Leukemia, Box 428, The University of Texas M.D.
Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX
77030, U.S.A. (e-mail: sfaderl@mdanderson.org).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Novel treatments for myelodysplastic syndromes (MDS) are reviewed.
Clinical features, diagnosis, classification, prognostic factors and
biology of MDS are briefly discussed. Treatment is reviewed with

reference to supportive care, hematopoietic growth factors, immunomodulation, farnesyl transferase inhibitors (FTI), **imatinib**, angiogenesis inhibitors, anti-tumor necrosis factor-alpha (anti-TNF-alpha) therapies, arsenicals, epigenetic therapy, high-intensity therapy, chemotherapy and stem cell transplantation. Efficacy, results of clinical trials, doses and toxicity are discussed.

L89 ANSWER 40 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2004-42053 DRUGU T P
 TITLE: New nucleoside analogs in the treatment of hematological disorders.
 AUTHOR: Szafraniec S I; Stachnik K J; Skierski J S
 CORPORATE SOURCE: Nat.Inst.Public-Health-Warsaw
 LOCATION: Warsaw, Pol.
 SOURCE: Acta Pol.Pharm. (61, No. 3, 223-32, 2004) 84 Ref.
 CODEN: APPHAX ISSN: 0001-6837
 AVAIL. OF DOC.: Flow Cytometry Laboratory, National Institute of Public Health, 30/34 Chelmska Str, 00-725 Warsaw, Poland. (J.S.S.). (e-mail: skierski@il.waw.pl).
 LANGUAGE: English
 DOCUMENT TYPE: Journal
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature
 AB The new nucleoside analogs (tezacitabine, **troxacitabine**, clofarabine, nelarabine, decitabine, 2'-C-cyano-2'-d-1-beta-D-arabino pentofuranosylcytosine (CNDAC) and 3'ethynylocytidine (ECyD) in the treatment of hematological disorders are reviewed. The mechanism of action, preclinical trials and clinical trials of tezacitabine, **troxacitabine**, clofarabine, nelarabine, decitabine and CNDAC are described.

L89 ANSWER 41 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2004-21310 DRUGU T P S
 TITLE: **Troxacitabine.**
 AUTHOR: Gourdeau H; Jolivet J
 CORPORATE SOURCE: ShireBioChem
 LOCATION: Quebec, Que., Can.
 SOURCE: Bull.Cancer (91, No. 3, 213-18, 2004) 2 Fig. 1 Tab. 43 Ref.
 CODEN: BUCABS ISSN: 0007-4551
 AVAIL. OF DOC.: ShireBioChem Inc., 275, boulevard Armand-Frappier, Quebec, Canada, H7V 4A7. (E-mail: henriettegourdeau@videotron.com).
 LANGUAGE: French
 DOCUMENT TYPE: Journal
 FIELD AVAIL.: AB; LA; CT
 FILE SEGMENT: Literature
 AB The antitumor activity of deoxycytidine analog **troxacitabine** (TX) in preclinical studies and phase I and II clinical trials is reviewed. Unlike lamivudine, gemcitabine and cytarabine (AC), TX has a non-natural beta-L stereochemical configuration. TX has a large spectrum of activity against in-vitro and animal cancer models, including vinblastine and doxorubicin resistant tumors but toxicity is greater in primates than rodents. TX has promising clinical activity against refractory solid tumors and acute leukemias (with AC, idarubicin and topotecan), dose-limiting side-effects are mainly hematological and cutaneous (eruption, stomatitis and hand-foot syndrome). Further studies are required.

L89 ANSWER 42 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2004-29719 DRUGU T
 TITLE: Emerging treatments in acute myeloid leukaemia.

AUTHOR: Kell J
CORPORATE SOURCE: Univ.Wales
LOCATION: Cardiff, U.K.
SOURCE: ; Expert Opinion Emerg.Drugs (9, No. 1, 55-71, 2004) 4 Fig. 3
Tab. 211 Ref.

CODEN: ; 4023
AVAIL. OF DOC.: University Hospital of Wales, Cardiff, CF14 4XW, Wales.
(e-mail: jonathan.kell@cardiffandvale.wales.nhs.uk).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB The scientific rationale of emerging treatments (**imatinib**, manumycin, alpha-hydroxyfarnesyl phosphonic acid, tipifarnib, SCH-66336, BMS-214662, anti-CD33 mAb, gemtuzumab ozogamicin, SU-5416, CEP-701, CT-53518, PKC-412, AG-1296, AG-1295, gemcitabine, clofarabine, **troxacitabine**, 5-azacytidine, decitabine, zebularine, depsipeptide, valproate) in acute myeloid leukemia (AML) is reviewed. The current treatments (daunorubicin, Ara-C, etoposide, idarubicin, mitoxantrone) for AML are discussed. The generally favorable side effect profiles of these drugs and the good oral bioavailability of at least some of the agents make them particularly attractive treatment options in the older population or patients not considered fit enough for intensive chemotherapy.

L89 ANSWER 43 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-10803 DRUGU P

TITLE: **Troxatyl** and STI571 combination therapy for chronic myeloid leukemia: preclinical in vitro and in vivo evaluation.

AUTHOR: Orsolic N; Giles F; Beran M; Cortes J; Albitar M; Kantarjian H; Verstovsek S

CORPORATE SOURCE: Univ.Texas-Syst.

LOCATION: Houston, Tex., USA

SOURCE: Blood (100, No. 11, Pt. 1, 786a, 2002) 2 Ref.

CODEN: BLOOAW ISSN: 0006-4971

AVAIL. OF DOC.: Leukemia, The University of Texas, MD Anderson Cancer Center, Houston, TX, U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The effects of **Troxatyl** (TX, **troxacitabine**) and **imatinib** (IM, STI-571) were investigated in-vitro in chronic myeloid leukemia (CML) KBM5 and KBM7 cells, IM-resistant sublines KBM5-R and KBM7-R, cells from patients with CML and in-vivo after i.p. administration in mice bearing KBM5 or KBM5-R cells. TX and IM showed a synergistic cytostatic activity both in in-vitro and in-vivo studies. In conclusion, the results show that TX has activity in late stage CML and that combining it with IM is a very reasonable clinical approach. (conference abstract: 44th Annual Meeting of the American Society of Hematology, Philadelphia, Pennsylvania, USA, 2002).

L89 ANSWER 44 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-17334 DRUGU T S

TITLE: Phase II study of **Troxatyl** in patients with chronic myeloid leukemia in blastic phase (CML-BP).

AUTHOR: Giles F; Feldman E; Cortes J; Faderl S; Larson R; Mamus S; Thomas D; Garcia Manero G; O'Brien S; Beran M; Talpaz M; Kantarjian H

CORPORATE SOURCE: Anderson-Cancer-Cent.; Univ.Chicago; Univ.Cornell
 LOCATION: Houston, Tex., New York, N.Y., Chicago, Ill.; Orlando, Fla.,
 USA

SOURCE: Blood (98, No. 11, Pt. 2, 258b, 2001) 1 Ref.
 CODEN: BLOOAW ISSN: 0006-4971

AVAIL. OF DOC.: UT MD Anderson Cancer Center, Houston, TX, U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The efficacy of **troxycitabine (Troxatyl)** was investigated in 26 patients with chronic myeloid leukemia in blastic phase (CML-BP) in a phase II study. Side-effects included skin rash, hyperbilirubinemia, hand foot syndrome, colitis, and Sweets syndrome. The result showed that **Troxatyl** had significant activity in these CML-BP patients. (conference abstract: 43rd Annual Meeting of the American Society of Hematology, Orlando, Florida, USA, 2001).

L89 ANSWER 45 OF 54 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-12589 DRUGU T S

TITLE: **Troxatyl** is effective in non-lymphoid blastic phase chronic myeloid leukemia (CML-BP).

AUTHOR: Giles F; Talpaz M; Bivins C; Jolivet J; Kantarjian H

CORPORATE SOURCE: Univ.Texas-Syst.

LOCATION: Houston, Tex., USA

SOURCE: Eur.J.Cancer (37, Suppl. 6, S35, 2001) 2 Ref.

CODEN: EJCAEL ISSN: 0964-1947

AVAIL. OF DOC.: University of Texas MD Anderson Cancer Center, Houston, TX,
 U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB The use of **troxycitabine (Troxatyl)** to treat 17 patients with non-lymphoid blastic phase chronic myeloid leukemia (CML-BP) is reported. Side-effects included rash, hand-foot syndrome and mucositis. Median survival was over 52 wk. **Troxatyl** as a single agent in CML-BP is under study in Phase II trial. (conference abstract: 11th European Cancer Conference, Lisbon, Portugal, 2001).

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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' -
 CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L89 ANSWER 46 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-048472 [05] WPIX

DOC. NO. CPI: C2005-016552

TITLE: Prevention/treatment/reduction of the occurrence of vascular stenosis or restenosis following angioplasty comprises administration of a platelet derived growth factor receptor inhibitor and a phosphoinositide-3 kinase pathway inhibitor.

DERWENT CLASS: B04 B05

INVENTOR(S): SUKHATME, V P

PATENT ASSIGNEE(S): (BETH-N) BETH ISRAEL DEACONESS MEDICAL CENT

COUNTRY COUNT: 108

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2004108130	A1	20041216	(200505)*	EN	48	A61K031-40	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE							
LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE							
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG							
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ							
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG							
US UZ VC VN YU ZA ZM ZW							

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004108130	A1	WO 2004-US17273	20040601

PRIORITY APPLN. INFO: US 2003-475295P 20030603

INT. PATENT CLASSIF.:

MAIN: A61K031-40

SECONDARY: A61K031-44; A61K031-519; A61K031-551

BASIC ABSTRACT:

WO2004108130 A UPAB: 20050124

NOVELTY - Prevention or treatment or reduction of the occurrence of vascular stenosis or restenosis following angioplasty comprises administration of a first compound (1) capable of inhibiting platelet derived growth factor receptor (PDGFR) and a phosphoinositide-3 kinase (PI3K) pathway inhibitor (2).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a pharmaceutical composition (A) comprising (1) and (2); and

(2) a kit comprising (1), (2), (3) and instructions for administration of (1), (2) and (3) to a patient diagnosed with or at risk of developing stenosis or restenosis following angioplasty.

ACTIVITY - Vasotropic.

MECHANISM OF ACTION - Platelet derived growth factor receptor beta (PDGFR- beta) inhibitor; Phosphoinositide-3 kinase (PI3K) pathway inhibitor.

USE - (1) along with (2) is useful in the prevention/treatment/reduction of the occurrence of vascular stenosis or restenosis (characterized by the migration of smooth muscle cells into the intima; the proliferation of vascular smooth muscle cells; or the deposition of extracellular matrix) following angioplasty and the use of a stent for treatment. (1) with (2) is also useful to reduce or prevent vascular smooth muscle cell hyperplasia (all claimed). The ability of (1) (**imatinib** mesylate) and (2) (rapamycin) to prevent migration of smooth muscle cells was tested using human aortic vascular smooth muscle cells. The results showed that the percentage inhibition was 70-80%.

ADVANTAGE - (1) and (2) acts synergistically.

Dwg.0/1

FILE SEGMENT:

CPI

FIELD AVAILABILITY:

AB; DCN

MANUAL CODES:

CPI: B01-A02; B01-B01; B01-B02; B02-C01; B02-R; B02-T; B03-H; B04-A03; B04-A06; B04-A08C2; B04-A10B; B04-C01B; B04-C01H; B04-G04; B04-G21; B04-H05A; B04-H19; B04-N02; B04-N06; B05-B01E; B05-B01J; B05-B01P; B06-A01; B06-A02; B06-D01; B06-D02; B06-D03; B06-D04; B06-D06; B06-D07; B06-D09;

B06-D17; B06-D18; B06-E05; B06-F03; B07-A01;
 B07-A02; B07-A03; B07-D03; B07-D04C; B07-D04D;
 B07-D05; B07-D08; B07-D12; B10-A09B; B10-B02D;
 B10-B02E; B10-B03B; B10-C03; B10-C04A; B10-C04D;
 B10-C04E; B10-E02; B14-D05C; B14-D06C; B14-D07A1;
 B14-F01G; B14-F02F2; B14-F04; B14-G02;
B14-H01B; B14-J04; B14-J05; B14-L06;
B14-S09

TECH

UPTX: 20050124

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: (1) is an N-phenyl-2-pyrimidine derivative, preferably **imatinib** mesylate. (1) inhibits PDGFR activity stimulated by a PDGF-BB ligand. (2) inhibits the biological activity of any protein on the phosphoinositide-3 kinase (PI3K)/Akt/ mammalian target of rapamycin (mTOR) signaling pathway and also inhibits the biological activity of mTOR. The stent is coated with (1) and (2). (1) and (2) are given in combination with a carrier. The treatment further comprises administration of at least one additional compound (3) such as an angiogenesis inhibitor, an anti-proliferative compound, an immunosuppressive compound, an anti-migratory compound, an anti-platelet agent and an anti-fibrotic compound. The angiogenesis inhibitor is an antibody; an antibody that binds vascular endothelial growth factor-A (VEGF-A); an antibody that binds a VEGF receptor and blocks VEGF binding; avastin; endostatin; angiostatin; restin; tumstatin; TNP-470; 2- methoxyestradiol; thalidomide; a peptide fragment of an antiangiogenic protein; canstatin; arrestin; a VEGF kinase inhibitor; CPTK787; SFH-1; an anti-angiogenic protein; thrombospondin-1; platelet factor-4; interferon-alpha; an agent that blocks TIE-1, TIE-2 or PIH12 signaling; an agent that blocks an extracellular vascular endothelial (VE) cadherin domain; an antibody that binds to an extracellular VE-cadherin domain; tetracycline; penicillamine; vinblastine; cytoxan; edelfosine; tegafur; uracil; curcumin; green tea; genistein; resveratrol; N-acetyl cysteine; captopril; a cyclooxygenase (cox-2) inhibitor; celecoxib or rofecoxib. The anti-proliferative compound is rapamycin; taxol; troglitazone; an agent that inhibits VEGF (preferably an antibody); an agent that inhibits bFGF (preferably an antibody); an antibody that binds bFGF-saporin; a statin; an angiotensin-converting enzyme (ACE) inhibitor; suramin; 17-beta-estradiol; atorvastatin; fluvastatin; lovastatin; pravastatin; simvastatin; cerivastatin; perindopril; quinapril; captopril; captopril; lisinopril; enalapril; fosinopril; cilazapril; ramipril; or a kinase inhibitor. The immunosuppressive compound is prednisone; FTY720; methylprednisolone; a-tocopherol; azathioprine; chlorambucil; cyclophosphamide; an antibody that binds to an interleukin-2 (IL-2) receptor or to cytotoxic T-lymphocyte associated antigen-4 (CTLA-4); methotrexate; mycophenolate mofetil; cyclosporine; an agent that interferes with macrophage function; an agent that inhibits P-selectin PSGL-1; very late antigen-4 (VLA-4); vascular cell adhesion molecule-1 (VCAM-1) or Mac-1 biological function; or FTY720. The anti-migratory compound is cyproheptadine; endothelin receptor antagonist; serotonin receptor antagonist; methysergide; bosentan; YM087; cyproheptadine; ketanserin; or anplag. The anti-platelet agent is aspirin; ticlopidine; cilostazol; dipyridamole; abciximab; clopidogrel; dipyridimole; a glycoprotein iib/iiia inhibitor; an adenosine reuptake inhibitor; an ADP inhibitor; eptifibatide; tirofiban; a phosphodiesterase III inhibitor; or ticlopidine. The anti-fibrotic compound is blocks tumor growth factor (TGF)-beta signaling or inhibits activation of plasminogen activator inhibitor-1 promoter activity; an antibody that binds to TGF-beta or to a TGF-beta receptor; an antibody that binds to TGF-beta receptor I, II, or III; a kinase inhibitor; an agent that blocks CTGF signaling; an agent that inhibits prolyl hydroxylase; an agent that inhibits procollagen C-proteinase; pirfenidone; silymarin; pentoxifylline; colchicines; embrel;

remicade; an agent that antagonizes TGF-beta; an agent that antagonizes CTGF; and an agent that inhibits VEGF. Preferred Composition: (A) further comprises at least one (3).

ABEX UPTX: 20050124

SPECIFIC COMPOUNDS - The use of **imatinib** mesylate is specifically claimed as (1). The use of rapamycin is specifically claimed as (2).

ADMINISTRATION - Administration of (1) and (2) is oral, parenteral, intravenous, subcutaneous or local. Administration of **imatinib** mesylate is 50-5000 (preferably 100-800) mg/day, orally.

L89 ANSWER 47 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2005-021162 [02] WPIX
 DOC. NO. CPI: C2005-006619
 TITLE: Combination useful for treating proliferative disease
 e.g. breast cancer comprises a chemotherapeutic agent and
 a histone deacetylase inhibitor.
 DERWENT CLASS: B05
 INVENTOR(S): ATADJA, P W; REMISZEWSKI, S W; TROGANI, N
 PATENT ASSIGNEE(S): (NOVS) NOVARTIS AG; (NOVS) NOVARTIS PHARMA GMBH
 COUNTRY COUNT: 108
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2004103358	A2	20041202	(200502)*	EN	43	A61K031-16	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE							
LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE							
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG							
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ							
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG							
US UZ VC VN YU ZA ZM ZW							

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004103358	A2	WO 2004-EP5433	20040519

PRIORITY APPLN. INFO: US 2003-472161P 20030521
 INT. PATENT CLASSIF.:

MAIN: A61K031-16
 SECONDARY: A61K031-4045; A61K031-4745; A61K031-513; A61K031-704;
 A61K031-7068; A61K045-06; **A61P035-00;**
A61P035-04

BASIC ABSTRACT:

WO2004103358 A UPAB: 20050107

NOVELTY - A combination comprises a chemotherapeutic agent (a1) and a histone deacetylase inhibitor (a2) in their free form, salt, or prodrugs, for simultaneous, concurrent, separate or sequential use.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a commercial package or product comprising (a1) together with instructions for use in combination with (a2), for treating a disease in a mammal, or (a2) together with instructions for use in combination with (a1), for treating a disease in a mammal.

ACTIVITY - Cytostatic; Respiratory-Gen; Nephrotropic; Antiangiogenic; Antipsoriatic; Antiarteriosclerotic; Antiinflammatory; Vasotropic;

Vulnerable.

MECHANISM OF ACTION - Vascular endothelial growth factor family of receptor tyrosine kinases (VEGFR) inhibitor or activator; Tumor growth inhibitor.

The antiproliferative effects of adding N-hydroxy-3-(4-(((2-hydroxyethyl)(2-(1H-indol-3-yl)ethyl)-amino)methyl)phenyl)-2E-2-propenamide (a2') simultaneously, 24 hours after, or 24 hours before adding the chemotherapeutic agent adriamycin to MDA-MB-435P cell line (human breast carcinoma) were examined. The combined effects were assessed using constant ratios of compound concentrations that were 8-fold, 4-fold, 2-fold, 1-fold, 0 fold, 0 fold and 0 fold of their respective IC50s. To examine whether the combinations were additive, synergistic or antagonistic, isobolograms were plotted and combination indices calculated using the commercial software program CalcuSyn. In isobolograms, the X intercepts indicate the concentrations of one drug which results in a given percentage of growth inhibition and the Y intercepts indicate the concentrations at which the other drug inhibited the growth of the cells. The data point that falls between the axes indicates the concentration of the drug combination that inhibits cell growth. The further above or below this data point deviates from the straight line joining the intercepts, the more antagonistic or synergistic the effect, respectively. Combination data points that fall on or close to the line joining the intercepts indicate additive effects.

Simultaneous incubation of MDA-MB-435P cells with adriamycin and (a2') or treatment with (a2') 24 hours prior to adding adriamycin produced isobologram combination data points close to the line joining the X and Y intercepts. The calculated combination indices were close to 1, indicating additive effects. However, treatment of MDA-MB-435P cells with adriamycin 24 hours prior to (a2') resulted in combination data points far below the line joining the intercepts, indicating strong synergy between the two drugs.

USE - For treatment of proliferative disease e.g. breast cancer, lung cancer, ovarian cancer, lymphoma, head and neck cancer and cancer of the esophagus, stomach, bladder, prostate, uterus and cervix; for treatment or prevention of proliferative diseases including premalignant lesions as well as both solid and undifferentiated malignancies (all claimed); for treatment of leukemias, hyperplasias, fibrosis (e.g. pulmonary or renal fibrosis), angiogenesis, psoriasis, atherosclerosis, and smooth muscle proliferation in blood vessels, such as stenosis or restenosis following angioplasty.

ADVANTAGE - The combination is more efficacious, provides synergistic and additive advantages, both for efficacy and safety; and provides lower safe dosage ranges of each component in the combination.

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B02-D; B06-H; B07-H; B08-H; B10-A09B; B10-A15;
B10-A18; B14-C03; B14-F01G; B14-F02F2; B14-F07;
B14-H01; B14-K01; B14-N10; B14-N17B;
B14-N17C; B14-S09

TECH UPTX: 20050107

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (a1) is DNA topoisomerase I inhibitor; DNA topoisomerase II inhibitor; microtubule active agent; or antimetabolites including agents which are inhibitors of thymidine production, inhibitors of vascular endothelial growth factor, DNA demethylating agents, or protein-tyrosine kinase inhibitors (such as discodermolides and epothilones), or salts or prodrugs of these. (a2) Is a compound of formula (I), preferably a compound of formula (Ia).
R1 = H, halo or 1-6C alkyl (preferably H);
R2 = U1 (preferably H or -CH2-CH2-OH);

U1 = H, 1-10C alkyl, 4-9C (hetero)cycloalkyl, 4-9C heterocycloalkylalkyl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, -(CH₂)_nC(O)R₆, -(CH₂)_nOC(O)R₆, amino acyl, HON-C(O)-CH=C(R₁)-aryl-alkyl- or -(CH₂)_nR₇; R₃, R₄ = H, 1-6C alkyl, acyl or acylamino (preferably H); or R₃+R₄ = C=O, C=S or C=NR₈; or NR₂R₃ = 4-9C heterocycloalkyl, heteroaryl, polyheteroaryl, non-aromatic polyheterocycle or a mixed aryl or non-aryl polyheterocycle ring; R₅ = H, T₁, acyl, aromatic polycycle, non-aromatic polycycle, mixed aryl and non-aryl polycycle, polyheteroaryl, non-aromatic polyheterocycle or mixed aryl and non-aryl polyheterocycle; T₁ = 1-6C alkyl, 4-9C (hetero)cycloalkyl, (hetero)aryl or (hetero)arylalkyl; X,Y = H, halo, 1-4C alkyl, NO₂, C(O)R₁, OR₉, SR₉, CN or NR₁₀R₁₁ (preferably H); R₆ = H, T₁, cycloalkylalkyl, OR₁₂ or NR₁₃R₁₄; R₇ = OR₁₅, SR₁₅, S(O)R₁₆, SO₂R₁₇, NR₁₃R₁₄ or NR₁₂SO₂R₆; R₈ = T₁, H, OR₁₅ or NR₁₃R₁₄; R₉ = 1-4C alkyl or C(O)-alkyl; R₁₀,R₁₁ = H or R₉; R₁₂ = T₁, H, 4-9C heterocycloalkylalkyl or mixed aryl and non-aryl polycycle; R₁₃, R₁₄ = T₁, H or amino acyl; R₁₃R₁₄N = 4-9C heterocycloalkyl, heteroaryl, polyheteroaryl, non-aromatic polyheterocycle or mixed aryl and non-aryl polyheterocycle; R₁₅ = T₁, H or (CH₂)_mZR₁₂; R₁₆ = T₁, polyheteroaryl or (CH₂)_mZR₁₂; R₁₇ = T₁, aromatic polycycle, polyheteroaryl or NR₁₃R₁₄; n, n₁, n₃, m = 0 - 6; n₂, n₃ = 0 - 6 (preferably 0 or 1); Z = O, NR₁₃, S or S(O); R₁₈ = H, halo, 12-6C alkyl, 3-7C cycloalkyl or (hetero)aryl (preferably H, fluoro, chloro, bromo, 1-4C alkyl, 3-7C cycloalkyl, phenyl or heteroaryl); R₂₀ = H, 1-6C alkyl, 3-9C cycloalkyl-1-6C alkyl, (hetero)aryl, (hetero)arylalkyl, acyl or sulfonyl; A₁ = 1 - 3 substituents selected from H, 1-6C alkyl, -OR₁₉, halo, alkylamino, aminoalkyl, halo or heteroarylalkyl; R₁₉ = H, T₁ or -(CH₂CH=CH(CH₃)(CH₂))₁₋₃H; p = 0 - 3; q, r = 0 - 5 (preferably 1 - 3); R'₂ = U₁ (preferably H or -(CH₂)_sCH₂OH); s = 1 - 3.

Provided that:

- (1) when n₁ is 1-6, each carbon atom can be optionally substituted with R₃ and/or R₄;
- (2) when one of n₂ and n₃ is 0, then the other of n₂ and n₃ is 1;
- (3) when q is 1 - 5, then r is 0; and
- (4) when q is 0, then r is 1 - 5.

ABEX

UPTX: 20050107

SPECIFIC COMPOUNDS - (a₁) Is adriamycin, epothilone B or D, 5-fluorouracil, camptothecin, gimatecan, **imatinib** (**Gleevec**), PTK787 (RTM; 1-(4-chloroanilino)-4-(pyridylmethyl)-phthalazine succinate), 5-Aza dC (decitabine) or 5-azacytidine. (a₂) is N-hydroxy-3-(4-(((2-hydroxyethyl)(2-(1H-indol-3-yl)ethyl)-amino)methyl)phenyl)-2E-2-propenamide (a₂'), N-hydroxy-3-(4-(((2-(1H-indol-3-yl)ethyl)amino)methyl)phenyl)-2E-2-propenamide or N-hydroxy-3-(4-(((2-(2-methyl-1H-indol-3-yl)ethyl)-amino)methyl)phenyl)-2E-2-propenamide

ADMINISTRATION - Administration is preferably oral in the form of a tablet, capsule or syrup, or as parenteral injections. E.g. adriamycin, 5-fluorouracil and camptothecin are each administered at 100-1500

(preferably 200-1000) mg/day in one or two doses.

L89 ANSWER 48 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2004-580619 [56] WPIX
 CROSS REFERENCE: 2004-561737 [54]; 2004-580620 [56]; 2004-580621 [56]
 DOC. NO. CPI: C2004-211614
 TITLE: Use of lonidamine in combination with one or more
 additional chemotherapeutic agents (e.g.
 2-deoxy-D-glucose) for the treatment of cancers like
 non-small-cell lung cancer, breast cancer, prostate
 cancer and colorectal cancer.
 DERWENT CLASS: B05
 INVENTOR(S): TIDMARSH, G
 PATENT ASSIGNEE(S): (THRE-N) THRESHOLD PHARM INC
 COUNTRY COUNT: 108
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2004064734	A2	20040805	(200456)*	EN	62	A61K000-00	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE							
LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE							
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG							
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ							
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG							
US UZ VC VN YU ZA ZM ZW							

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004064734	A2	WO 2004-US1138	20040116

PRIORITY APPLN. INFO: US 2003-458663P 20030328; US
 2003-441110P 20030117; US
 2003-442344P 20030123

INT. PATENT CLASSIF.:

MAIN: A61K000-00

BASIC ABSTRACT:

WO2004064734 A UPAB: 20040901

NOVELTY - Treatment of cancer comprises administration of lonidamine (I) in combination with one or more additional chemotherapeutic agents (II) to mammals.

ACTIVITY - Cytostatic; Antithyroid; Dermatological; Fungicide; Anti-HIV; Osteopathic; Cardiovascular-Gen.; CNS-Gen.; Gastrointestinal-Gen.

MECHANISM OF ACTION - HIF-1 alpha inhibitor; VegF inhibitor.

USE - Lonidamine (I) in combination with one or more of (II) is useful for the treatment of cancer (breast cancer, skin cancer, bone cancer, prostate cancer, liver cancer, lung cancer, brain cancer, cancer of the larynx, gall bladder, pancreas, rectum, parathyroid, thyroid, adrenal, neural tissue, head and neck, colon, stomach, bronchi, kidneys, basal cell carcinoma, squamous cell carcinoma of both ulcerating and papillary type, metastatic skin carcinoma, osteo sarcoma, Ewing's sarcoma, veticulum cell sarcoma, myeloma, giant cell tumor, small-cell lung tumor, islet cell tumor, primary brain tumor, acute and chronic lymphocytic and granulocytic tumors, hairy-cell tumor, adenoma, hyperplasia, medullary carcinoma, pheochromocytoma, mucosal neuronomas, intestinal

ganglioneuromas, hyperplastic corneal nerve tumor, marfanoid habitus tumor, Wilm's tumor, seminoma, ovarian tumor, leiomyomater tumor, cervical dysplasia and in situ carcinoma, neuroblastoma, retinoblastoma, soft tissue sarcoma, malignant carcinoid, topical skin lesion, mycosis fungoide, rhabdomyosarcoma, Kaposi's sarcoma, osteogenic and other sarcoma, malignant hypercalcemia, renal cell tumor, polycythemia vera, adenocarcinoma, glioblastoma multiforma, leukemias, lymphomas, malignant melanomas or epidermoid carcinomas) (claimed).

The effect of (I) in treating cancers was tested using biological assays. The results showed lonidamine as a highly useful agent in combination therapies for all solid tumors.

ADVANTAGE - Cancer is treated by administering lonidamine or a lonidamine analog at a lower dose that may be continued to be administered for weeks to months while limiting or eliminating the unwanted, albeit usually mild, side effects reported for higher doses of lonidamine (principally myalgia and testicular pain).

Dwg.0/4

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; DCN

MANUAL CODES: CPI: B01-A02; B01-B01; B01-D02; B02-B; B02-C01; B02-D; B02-N; B02-O; B02-P; B02-R; B02-S; B02-T; B04-C01B; B04-G21; B04-L05; B05-A03B; B06-A01; B06-A02; B06-A03; B06-D04; B06-D05; B06-D06; B06-D08; B06-D09; B06-D11; B06-D16; B06-D18; B06-E05; B06-F03; B07-A02; B07-A04; B07-D01; B07-D04C; B07-D09; B07-D12; B07-D13; B07-E02; B07-F01; B08-D02; B08-D03; B10-A07; B10-A13D; B10-A16; B10-B01A; B10-B02A; B10-B02E; B10-B02J; B10-B03B; B10-B04; B14-H01; B14-L06; B14-S09

TECH UPTX: 20040901

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components:

Chemotherapeutic agent (II) is selected from busulfan, improsulfan, piposulfan, benzodepa, carboquone, 2-deoxy-D-glucose, meturedopa, uredepa, altretamine, imatinib, triethylenemelamine, triethylenephosphoramidate, triethylenethiophosphoramidate, trimethylolomelamine, chlorambucil, chlornaphazine, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard, carmustine, chlorozotocin, fotemustine, nimustine, ranimustine, dacarbazine, mannomustine, mitobronitol, mitolactol, pipobroman, aclacinomycins, actinomycin F(1), anthramycin, azaserine, bleomycin, cactinomycin, carubicin, carzinophilin, chromomycin, dactinomycin, daunorubicin, daunomycin, 6-diazo-5-oxo-1-norleucine, mycophenolic acid, nogalamycin, olivomycin, peplomycin, plicamycin, porfiromycin, puromycin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin, denopterin, pteropterin, trimetrexate, fludarabine, 6-mercaptopurine, thiamiprine, thioguanine, ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, 5-fluorouracil, tegafur, L-asparaginase, pulmozyme, aceglatone, aldophosphamide glycoside, aminolevulinic acid, amsacrine, bestabucil, bisantrene, carboplatin, defofamide, demecolcine, diaziquone, elfomithine, elliptinium acetate, etoglucid, flutamide, gallium nitrate, hydroxyurea, interferon-alpha, interferon-beta, interferon-gamma, interleukin-2, lentinan, mitoguazone, mitoxantrone, mopidamol, nitracrine, pentostatin, phenamet, pirarubicin, podophyllinic acid, 2-ethylhydrazide, procarbazine, razoxane, sizofiran, spirogermanium, paclitaxel, tamoxifen, teniposide, tenuazonic acid, triaziquone, 2',2',2-trichlorotriethylamine, urethan, vinblastine or vincristine) (preferably gemcitabine, a taxane or 2-deoxy-D-glucose). (II) is both 2-deoxy-2-glucose and one or more agents of cisplatin, carboplatin, taxol, taxotere, cytoxan, vincristine,

adriamycin, captosar, 5-fluorouracil, levamisole, prednisone, mitoxantrone, herceptin or vinorelbine (preferred).

Preferred Method: For the treatment of non-small-cell lung cancer, (I) is co-administered with either cisplatin or carboplatin together with an anti-cancer agent (taxol, taxotere, gemcitabine or vinorelbine).

For the treatment of breast cancer, (I) is co-administered with either taxol or taxotere and herceptin; or cytoxan and 5-fluorouracil and either adriamycin or methotrexate.

For the treatment of prostate cancer, (I) is co-administered with either prednisone or taxotere, and optionally with mitoxantrone (if prednisone is administered).

For the treatment of colorectal cancer, (I) is co-administered with either captosar or 5-fluorouracil and levamisole.

For the treatment of ovarian cancer, either (I) is co-administered with cisplatin or carboplatin, together with either taxol or taxotere; or (I) is co-administered with cisplatin or carboplatin; or cytoxan, vincristine, and prednisone, and optionally together with adriamycin.

For the treatment of cancers (particularly head or neck cancer), lonidamine or its analog in combination is administered with hyperfractionated radiation therapy. (I) can also be administered with a HIF-1 alpha inhibitor or a VegF inhibitor (particularly avastin to treat colon cancer, pancreatic cancer or renal cell carcinoma).

ABEX UPTX: 20040901

ADMINISTRATION - Administration of (I) is greater than 300 and less than 500 mg/day (low dosage), orally, parenterally, transdermally, rectally or by inhalation spray or intraprostatic injection.

L89 ANSWER 49 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-460982 [43] WPIX

DOC. NO. CPI: C2004-172134

TITLE: Use of cell cycle checkpoint activator and oncogenic kinase modulator for treatment of cancer e.g. lung cancer, malignant melanoma and childhood leukemia.

DERWENT CLASS: B02

INVENTOR(S): LI, C; LI, Y

PATENT ASSIGNEE(S): (ARQU-N) ARQULE INC

COUNTRY COUNT: 107

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2004050033	A2	20040617	(200443)*	EN	40	A61K000-00	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE							
LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK							
DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP							
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG							
PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ							
VC VN YU ZA ZM ZW							
AU 2003293333	A1	20040623	(200472)			A61K000-00	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004050033	A2	WO 2003-US38405	20031202
AU 2003293333	A1	AU 2003-293333	20031202

FILING DETAILS:

PATENT NO	KIND	PATENT NO
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AU 2003293333	A1 Based on	WO 2004050033

PRIORITY APPLN. INFO: US 2002-430288P 20021202

INT. PATENT CLASSIF.:

MAIN: A61K000-00

BASIC ABSTRACT:

WO2004050033 A UPAB: 20040709

NOVELTY - Treatment of cancer comprises administration of a cell cycle checkpoint activator (A) or its derivative or analog, and an oncogenic kinase modulator (B).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit for the treatment of a malignancy comprising separate vials containing beta -lapachone and (B), with instructions for administering beta -lapachone first.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Cell cycle checkpoint activator; Oncogenic kinase modulator.

USE - (A) and (B) are useful in the treatment of lung cancer, breast cancer, colon cancer, ovarian cancer, prostate cancer, malignant melanoma, non-melanoma skin cancers, hematologic tumors, hematologic tumors, hematologic malignancies, childhood leukemia, childhood lymphomas, multiple myeloma, Hodgkin's disease, lymphomas of lymphocytic origin, lymphomas of cutaneous origin, acute leukemia, chronic leukemia, acute lymphoblastic leukemia, acute myelocytic leukemia, chronic myelocytic leukemia, plasma cell neoplasm, lymphoid neoplasm, cancers associated with AIDS or preferably multiple myeloma, chronic myelogenous leukemia, pancreatic cancer or non-small cell lung cancer in human (claimed).

The ability of (B) (2 micro M) along with (A) (20 micro M) to treat cancer was assessed in K562 cells (a human chronic myelogenous leukemia (CML) cell line). Results showed that the percentage viability of cells was found to be 3.8%.

ADVANTAGE - (A) and (B) are synergistic.

Dwg.0/2

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; DCN

MANUAL CODES: CPI: B06-A02; B07-D04C; B07-D11; B07-D12; B14-D06;
B14-H01; B14-L01; B14-S09

TECH UPTX: 20040709

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (B) is a tyrosine kinase modulator, which is an epidermal growth factor receptor signal transduction pathway modulator or preferably a breakpoint cluster region (Bcr)-Abl signal transduction pathway modulator. (A) further comprises a pharmaceutically acceptable water solubilizing carrier molecule such as poloxamer, povidone K17, povidone K12, tween 80, ethanol, cremophor/ethanol, polyethylene glycol 400, propylene glycol, trappsol, or alpha-, beta- or delta-cyclodextrin. (A) is contained in a first vial and (B) is contained in a second vial.

Preferred Method: (B) is administered simultaneously with, sequentially, preceding or preferably following (within 24 hours) administration of (A).

ABEX UPTX: 20040709

SPECIFIC COMPOUNDS - The use of beta-lapachone is specifically claimed as (A). The use of **imatinib** is specifically claimed as (B).

ADMINISTRATION - Dosage of (A) is 100 - 500000 (preferably 10000 - 150000) ug/kg/day, and of (B) is 10 - 2000 (preferably 250) mg/day, and administration is intravenous, intraperitoneal or preferably oral.

L89 ANSWER 50 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-440878 [41] WPIX
 DOC. NO. CPI: C2004-165247
 TITLE: Use of indolinone compounds which are receptor tyrosine kinase inhibitors, in combination with at least one chemotherapeutic agent for treatment of cancer, e.g. colon cancer and non-small cell lung cancer.
 DERWENT CLASS: B02
 INVENTOR(S): ABRAMS, T; CHERRINGTON, J; MURRAY, L; PRYER, N; CHERRINGTON, J M
 PATENT ASSIGNEE(S): (SUGE-N) SUGEN INC
 COUNTRY COUNT: 107
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2004045523	A2	20040603	(200441)*	EN	87	A61K000-00	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE							
LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE							
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG							
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM							
PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US							
UZ VC VN YU ZA ZM ZW							
US 2004152759	A1	20040805	(200452)			A61K031-4439	
AU 2003290943	A1	20040615	(200470)			A61K000-00	
NL 1024779	C2	20041109	(200505)			A61K031-404	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004045523	A2	WO 2003-US36526	20031114
US 2004152759	A1 Provisional	US 2002-426386P	20021115
		US 2003-712296	20031114
AU 2003290943	A1	AU 2003-290943	20031114
NL 1024779	C2	NL 2003-1024779	20031114

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003290943	A1 Based on	WO 2004045523

PRIORITY APPLN. INFO: US 2002-426386P 20021115; US
 2003-712296 20031114

INT. PATENT CLASSIF.:

MAIN: A61K000-00; A61K031-404; A61K031-4439
 SECONDARY: A61K031-405; A61K031-4745; A61K031-513; A61K031-704;
 A61K033-24; **A61P035-00**

BASIC ABSTRACT:

WO2004045523 A UPAB: 20040629

NOVELTY - Treatment of cancer comprises administration of indolinone compounds (I) or their salts, hydrates or solvates in combination with at least one chemotherapeutic agent (A) (e.g. microtubule interference agents, topoisomerase inhibitors, alkylating agents and/or kinase inhibitors).

DETAILED DESCRIPTION - Treatment of cancer comprises administration of indolinone compounds of formula (I) or their salts, hydrates or solvates in combination with at least one chemotherapeutic agent (A) (e.g. microtubule interference agents, topoisomerase inhibitors, alkylating

agents, thymidylate synthase inhibitors, irreversible steroidal aromatase inactivators, anti-metabolites, pyrimidine antagonists, purine antagonists, ribonucleotide reductase inhibitors and/or kinase inhibitors).

R = H, OH, (cyclo)alkyl, (hetero)aryl, alkoxy, heterocyclic or NH₂;
 R₁ = halo, (halo)alkyl, (halo)alkoxy, cycloalkyl, heterocyclic, OH,
 C(O)-R₈, NR₉R₁₀, NR₉C(O)-R₁₂ or C(O)NR₉R₁₀;
 R₂ = alkyl, (hetero)aryl, C(O)-R₈ or SO₂R';
 R' = alkyl, (hetero)aryl, NR₉R₁₀ or alkoxy;
 R₅ = H, (halo)alkyl, cycloalkyl, (hetero)aryl, heterocyclic, OH,
 C(O)-R₈ or (CHR)rR₁₁;

X = O or S;

p, r = 0-3;

q = 0-2;

R₈ = OH, (hetero)aryl, alkoxy, (cyclo)alkyl or heterocyclic;

R₉, R₁₀ = H, (amino)alkyl, (hetero)aryl, cycloalkyl or heterocyclic;

or

NR₉R₁₀ = ring with C, N, O or S;

R₁₁ = OH, NH₂, mono/di-substituted amino, (hetero)aryl, alkoxy, (cyclo)alkyl or heterocyclic;

R₁₂ = (hetero)aryl, alkoxy, (cyclo)alkyl or heterocyclic;

Z = OH, O-alkyl or NR₃R₄;

R₃, R₄ = H, (hetero)aryl, (cyclo)alkyl or heterocyclic; or

NR₃R₄ = ring with CH₂, N, O or S, or group of formula (i);

Y = CH₂, O, N or S; or

Q = C or N;

n = 0-4; and

m = 0-3.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Tyrosine kinase inhibitor; Topoisomerase inhibitor; Thymidylate synthase inhibitor; Irreversible steroidal aromatase inactivator; Pyrimidine antagonist; Purine antagonist; Ribonucleotide reductase inhibitor.

USE - (I) is useful in the treatment of cancers (particularly colon cancer and non-small cell lung cancer) (claimed).

ADVANTAGE - The combination of (I) and (A) are administered at a dose lower than the current standard, providing beneficial efficacy and enhanced effect in the treatment of cancer and reducing the toxicity of (A). The enhanced anti-tumor efficacy of compounds (I) in combination with docetaxel was determined using MX-1 human breast carcinoma subcutaneous tumor model with (I) alone as control. The results showed that combined treatment with (I) and docetaxel resulted in a percentage inhibition value of 82 (53 for control).

Dwg.0/8

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; GI; DCN

MANUAL CODES: CPI: B01-B03; B02-Z; B04-A07A; B04-B03A; B04-G01;
 B04-G21; B04-M01; B05-A03B; B05-B01J; B06-D01;
 B06-H; B07-H; B10-A09B; B10-A13D; B10-B01A;
 B10-B02A; B14-D03; **B14-H01**; B14-L06;
B14-S09

TECH UPTX: 20040629

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The salt of (I) is a malate salt. (A) are taxanes, vinca alkaloids, topoisomerase I inhibitors or topoisomerase II inhibitors (preferably paclitaxel, docetaxel (taxotere), vinblastine, vincristine, vindesine, irinotecan, doxorubicin, epirubicin, leucovorin, etoposide, teniposide, idarubicin, gemcitabine, daunorubicin, carboplatin, cisplatin, oxaliplatin, chlorambucil, melphalan, cyclophosphamide, ifosfamide, temozolomide, thiotepa, mitomycin C, busulfan, carmustine, lomustine, 5-fluorouracil,

capecitabine, exemestane, methotrexate, trimetrexate, fluorouracil, fluorodeoxyuridine, azacytidine, mercaptopurine, thioguanine, pentostatin, cytarabine, fludarabine, hydroxyurea, bevacizumab, cetuximab, gefitinib and imatinib). For the treatment of non-small cell lung cancer, (I) is administered with carboplatin and paclitaxel, or with carboplatin, docetaxel, cisplatin, gemcitabine, 5-fluorouracil, irinotecan or leucovorin. For the treatment of colon cancer, (I) is administered with 5-fluorouracil, oxaliplatin or leucovorin.

ABEX

UPTX: 20040629

SPECIFIC COMPOUNDS - The use of 9 compounds (I) are specifically claimed, i.e. 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylamino-ethyl)-amide, 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide, 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-morpholin-4-yl-ethyl)-amide, (S)-5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide, (R)-5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide, 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide, 5-(5-chloro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl)-amide, 5-(5-fluoro-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-ethylamino-ethyl)-amide and 3-(3,5-dimethyl-4-(4-morpholin-4-yl-piperidine-1-carbonyl)-1H-pyrrol-2-methylene)-5-fluoro-1,3-dihydro-indol-2-one.

ADMINISTRATION - Administration of (I) is 25-1500 (preferably 3 mg/m²/day), orally or parenterally.

DEFINITIONS - Preferred Definitions:

R1 = halo (preferably F or Cl);
 Z = NR₃R₄ or group of formula (i);
 R₃, R₄ = lower alkyl or preferably a morpholine ring;
 Y = CH₂;
 R₂ = methyl (bonded at 3 and 5 positions);
 m = 0;
 n, q = 2; and
 p = 1.

L89 ANSWER 51 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-365099 [34] WPIX

DOC. NO. CPI: C2004-137846

TITLE: Pharmaceutical composition, useful for the treatment, prevention and management of a myelodysplastic syndrome, comprises an immunomodulatory compound and optionally a carrier and a second active ingredient.

DERWENT CLASS: B02

INVENTOR(S): ZELDIS, J B

PATENT ASSIGNEE(S): (CELG-N) CELGENE CORP; (ZELD-I) ZELDIS J B

COUNTRY COUNT: 103

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
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WO 2004035064	A1	20040429	(200434)*	EN	47	A61K031-724	
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RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
 LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM
ZW

AU 2003228508 A1 20040504 (200467) A61K031-724
US 2004220144 A1 20041104 (200473) A61K038-19
EP 1487461 A1 20041222 (200501) EN A61K031-724

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004035064	A1	WO 2003-US11323	20030413
AU 2003228508	A1	AU 2003-228508	20030413
US 2004220144	A1 Provisional	US 2002-418468P	20021015
		US 2003-411649	20030411
EP 1487461	A1	EP 2003-726262	20030413
		WO 2003-US11323	20030413

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003228508	A1 Based on	WO 2004035064
EP 1487461	A1 Based on	WO 2004035064

PRIORITY APPLN. INFO: US 2002-418468P 20021015; US
2003-411649 20030411

INT. PATENT CLASSIF.:

MAIN: A61K031-724; A61K038-19

SECONDARY: A61K031-496; A61K031-7056

BASIC ABSTRACT:

WO2004035064 A UPAB: 20040527

NOVELTY - A pharmaceutical composition comprises an immunomodulatory compound or its salt, solvate, hydrate, stereoisomer, clathrate or prodrug and optionally a carrier and a second active ingredient.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) A method of reducing or avoiding an adverse effect associated with the administration of a second active ingredient in a patient suffering from a myelodysplastic syndrome involving administering the second active ingredient and the immunomodulatory compound;

(2) A single dosage unit form comprising the immunomodulatory compound and the second active ingredient;

(3) A kit comprising a composition containing the immunomodulatory compound and umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow and optionally the second active ingredient; and

(4) Treating, preventing and managing a myelodysplastic syndrome involving determining if the patient has a Del5q31-33 abnormality and administering the immunomodulatory compound.

ACTIVITY - Antianemic; Neuroprotective; Cytostatic; Immunosuppressive.

MECHANISM OF ACTION - Cytokine production modulator.

An in vitro study was carried out to investigate the effect of 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione (Ia) on the inhibition of TNF- α production following LPS-stimulation of human PBMC according to the methods described by Muller et al.,

Bioorg.Med.Chem.Lett.9:1625-1630, 1999) The test compound showed an IC50 value of 25.9 ng/ml.

USE - The composition is useful for the treatment, prevention and management of primary or secondary myelodysplastic syndrome in patients having a De15q31-33 abnormality. The myelodysplastic syndrome includes refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation and chronic myelomonocytic leukemia (Claimed). The composition is also useful in combination with transplantation therapy to reduce the risk of graft versus host disease.

ADVANTAGE - The components of the composition show synergism

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B01-B02; B02-Z; B03-A; B04-G21; B04-H04A; B04-H04C;
B04-H08; B04-N06; B06-D02; B06-D03; B06-D09;
B06-D18; B06-E05; B07-A02A; B07-D04C; B07-D11;
B07-D12; B10-A15; B10-C04C; B14-F03; B14-G02;
B14-G03; **B14-H01A**; B14-N16;
B14-S09

TECH UPTX: 20040527

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compound: The immunomodulatory compound is of formula (I) or (II).

X and Y = CO or CH₂;

R₂ = H or lower alkyl;

R₁ = H, 1-8C alkyl, 3-7C cycloalkyl, 2-8C alkenyl, 2-8C alkynyl, benzyl, aryl, 0-4C alkyl-(1-6C)heterocycloalkyl, 0-4C alkyl-2-5C heteroaryl, C(O)R₃, C(S)R₃, C(O)OR₄, 1-8C alkyl-N(R₆)₂, 1-8C alkyl-OR₅, 1-8C alkyl-C(O)OR₅, C(O)NHR₃, C(S)NHR₃, C(O)NR₃R₃', C(S)NR₃R₃' or 1-8C alkyl-O(CO)R₅;

R₂' = H, F, benzyl, 1-8C alkyl, 2-8C alkenyl or 2-8C alkynyl;

R₃ and R₃' = 1-8C alkyl, 3-7C cycloalkyl, 2-8C alkenyl, 2-8C alkynyl, benzyl, aryl, 0-4C alkyl-(1-6C)heterocycloalkyl, 0-4C alkyl-(2-5C)heteroaryl, 0-8C alkyl-N(R₆)₂, 1-8C alkyl-OR₅, 1-8C alkyl-C(O)OR₅, 1-8C alkyl-O(CO)R₅ or C(O)OR₅;

R₄ = 1-8C alkyl, 2-8C alkenyl, 2-8C alkynyl, 1-4C alkyl-OR₅, benzyl, aryl, 0-4C alkyl-1-6C heterocycloalkyl or 0-4C alkyl-2-5C heteroaryl;

R₅ = 1-8C alkyl, 2-8C alkenyl, 2-8C alkynyl, benzyl, aryl or 2-5C heteroaryl;

R₆ = H, 1-8C alkyl, 2-8C alkenyl, 2-8C alkynyl, benzyl, aryl, 2-5C heteroaryl or 0-8C alkyl-C(O)OR₅;

R₆+R₆ = heterocycloalkyl;

n = 0 or 1;

a = chiral-carbon center.

Provided that one of X and Y is CO and the other of X and Y is CO or CH₂.

The immunomodulatory compound is selected from:

- (1) a cyano or carboxy derivative of a substituted styrene;
- (2) a 1-Oxo-2-(2,6-dioxo-3-fluoropiperidin-3-yl)isoindoline derivative;
- (3) a 1,3-dioxo-2-(2,6-dioxo-3-fluoropiperidine-3-yl)isoindoline derivative; and
- (4) a tetra-substituted 2-(2,6-dioxopiperidin-3-yl)-1-oxoisoindoline derivative.

Preferred components: The second active ingredient improves blood cell production and is selected from:

- (1) cytokine;
- (2) hematopoietic growth factor;
- (3) anti-cancer agent;
- (4) antibiotic;
- (5) proteasome inhibitor;
- (6) immunosuppressive agent (preferably etanercept, imatinib,

anti-TNF-alpha antibody, infliximab, G-CSF, GM-CSF, EPO, topotecan, pentoxifyline, ciprofloxacin, irinotecan, vinblastine, dexamethasone, interleukin(IL)-2, IL-8, IL-18, ara-C, vinorelbine, isotretinoin, 13-cis-retinoic acid or their active mutant or derivative).

Preferred Kit: The kit additionally comprises a device for the administration of the composition or the single unit dosage form.

ABEX UPTX: 20040527

SPECIFIC COMPOUNDS - The use of 4-(amino)-2-(2,6-dioxo(3-piperidyl)-isoindoline-1,3-dione; and 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione (Ia) is specifically claimed as the immunomodulatory compounds.

ADMINISTRATION - The immunomodulatory compound is administered during or after transplanting umbilical cord blood, placental blood, peripheral blood stem cell, hematopoietic stem cell preparation or bone marrow in a patient.

The single dosage unit form is administered intravenously or subcutaneously (all claimed). The composition is administered orally, mucosally (e.g. nasally, sublingually, vaginally, buccally or rectally) or parenterally (e.g. subcutaneously, intravenously, through bolus injection, intramuscularly or intraarterially), transdermally or transcutaneously. The immunomodulatory compound is administered in a dosage of 0.10 - 150 mg or 0.1, 1, 2, 5, 7.5, 10, 12.5, 15, 17.5, 20, 25, 50, 100, 150 or 200 mg. The second active ingredient is administered intravenously or subcutaneously in a dosage of 1 - 1000 (preferably 5 - 500, especially 10 - 350, particularly 50 - 200) mg.

L89 ANSWER 52 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
 ACCESSION NUMBER: 2004-340814 [31] WPIX
 DOC. NO. CPI: C2004-129432
 TITLE: Use of 4-(4-methylpiperazin-1-ylmethyl)-N-(4-methyl-3-(4-pyridin-3-ylpyrimidin-2-ylamino)phenyl)benzamide in the manufacture of medicament for treatment of cancer expressing breast cancer resistance protein.
 DERWENT CLASS: B03
 INVENTOR(S): HOUGHTON, P J; TRAXLER, P
 PATENT ASSIGNEE(S): (NOVS) NOVARTIS AG; (NOVS) NOVARTIS PHARMA GMBH; (SJUD-N) ST JUDE CHILDREN'S RES HOSPITAL
 COUNTRY COUNT: 93
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2004032925	A1	20040422	(200431)*	EN	19	A61K031-44	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR							
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LT LU LV MA MD MK MN MX NI NO NZ OM PG PH PL PT RO RU SC SE SG SK SY TJ TM TN TR TT UA US UZ VC VN YU ZA ZW							
AU 2003273986	A1	20040504	(200465)			A61K031-44	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004032925	A1	WO 2003-EP11271	20031010
AU 2003273986	A1	AU 2003-273986	20031010

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003273986	A1 Based on	WO 2004032925

PRIORITY APPLN. INFO: US 2002-417915P 20021011

INT. PATENT CLASSIF.:

MAIN: A61K031-44
SECONDARY: A61K031-137; A61K031-335; A61K031-4745; A61K031-704;
A61P035-00

BASIC ABSTRACT:

WO2004032925 A UPAB: 20040514

NOVELTY - In the manufacture of medicament for the treatment of cancer expressing breast cancer resistance protein (BCRP), 4-(4-methylpiperazin-1-ylmethyl)-N-(4-methyl-3-(4-pyridin-3-ylpyrimidin-2-ylamino)phenyl)benzamide (**imatinib**) or its salts are used.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for treatment of the cancer that expresses BCRP, involving administration of an anticancer agent and **imatinib** or its salts.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Breast cancer resistance protein inhibitor; Topoisomerase I Inhibitor.

Human osteosarcoma cells were incubated with topotecan alone for control and a combination of topotecan and **imatinib** (1 micro M) for test. The results indicated that the IC50 value for test/control was 35/254 nM respectively.

USE - In manufacture of medicament for treatment of cancer expressing and over expressing BCRP; inhibiting BCRP; improving the absorption of orally administered anticancer agent by inhibiting BCRP in a patient having cancer (e.g. colon cancer, breast cancer, liver cancer, ovarian cancer, fibrosarcoma, myeloma, acute myeloid leukemia (AML), gastric cancer or non-small cell lung cancer) (claimed).

ADVANTAGE - **Imatinib** improves the absorption of an orally administered anticancer agent and prevents or reverses resistance to it. Also it inhibits breast cancer resistance protein.

Dwg.0/0

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; DCN

MANUAL CODES: CPI: B02-D; B02-T; B04-C02; B04-C03C; B05-B01B; B06-E05;
B07-D04C; B07-D11; B07-D12; B08-D02; B14-D09;
B14-H01; B14-L06; B14-S09

TECH UPTX: 20040514

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The anticancer agent is anthracycline cytotoxic agent or camptothecin-derived topoisomerase I inhibitor (preferably mitoxanthrone, doxorubicin, topotecan, irinotecan, 7-ethyl-10-hydroxycamptothecin (SN-38), 9-aminocamptothecin, 9-nitrocamptothecin, lurtotecan, diflomotecan, BAY38-3441, 7-(2-trimethylsilyl)ethylcamptothecin, 10-hydroxy-7-tert-butyltrimethylsilylcamptothecin, CT2016, DE310, T-0128 or PROTHECAN (RTM; PEG-camptothecin) (especially topotecan, irinotecan, SN-38, mitoxanthrone or doxorubicin)). **Imatinib** is in the form of the mesylate salt.

ABEX UPTX: 20040514

ADMINISTRATION - The administration is oral (claimed). The dosage is 100 - 1000 (preferably 400 - 600) mg/day.

EXAMPLE - No relevant example given.

L89 ANSWER 53 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-315711 [29] WPIX
DOC. NO. CPI: C2004-119711

TITLE: Composition useful for inducing apoptosis in cancer cells, e.g. chronic myeloid leukemia cells, comprises a tyrosine kinase inhibitor and a histone deacetylase inhibitor.

DERWENT CLASS: B05

INVENTOR(S): BHALLA, K N; NIMMANAPALLI, R

PATENT ASSIGNEE(S): (UYSF-N) UNIV SOUTH FLORIDA

COUNTRY COUNT: 105

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2004026234	A2	20040401	(200429)*	EN	12	A61K000-00	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS							
LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK							
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR							
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH							
PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN							
YU ZA ZM ZW							
US 2004127571	A1	20040701	(200444)			A61K031-19	
AU 2003270668	A1	20040408	(200462)			A61K000-00	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004026234	A2	WO 2003-US28964	20030919
US 2004127571	A1 Provisional	US 2002-319563P	20020919
		US 2003-605283	20030919
AU 2003270668	A1	AU 2003-270668	20030919

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003270668	A1 Based on	WO 2004026234

PRIORITY APPLN. INFO: US 2003-605283 20030919; US 2002-319563P 20020919

INT. PATENT CLASSIF.:

MAIN: A61K000-00; A61K031-19

BASIC ABSTRACT:

WO2004026234 A UPAB: 20040505

NOVELTY - A composition for inducing apoptosis in cancer cells comprises a tyrosine kinase inhibitor and a histone deacetylase inhibitor.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Apoptosis inducer; Tyrosine kinase inhibitor; Histone deacetylase inhibitor.

The effect of tyrosine kinase inhibitor, e.g. **imatinib** mesylate (a), alone and in combination with histone deacetylase inhibitor, e.g. suberoylanilide hydroxamic acid (b), was determined in Lama-84 cells. The cells were exposed for 48 days and the % apoptosis was determined. The results showed that the combination of (a) and (b) was effective on an exposure-dependent basis and induced more apoptosis of the cells compared to the treatment with (a) or (b) alone.

USE - For inducing apoptosis in cancer cells (such as leukemia cells and **imatinib** mesylate refractory cells); and for potentiating a cytotoxic effect of a tyrosine kinase inhibitor by contacting target cells with a histone deacetylase inhibitor (claimed), in the treatment of e.g.

accelerated and blast phases of chronic myeloid leukemia and Bcr-Abl positive acute lymphoblastic leukemia.

ADVANTAGE - The tyrosine kinase inhibitor inhibits binding of ATP with Bcr-Abl protein; preventing the Bcr-Abl protein from carrying out its kinase activity for apoptosis inhibition. The histone deacetylase inhibitor induces apoptosis by causing hyper-acetylation of the amino terminal lysine residues of core nucleosomal histones and of specific transcriptional regulators. The histone deacetylase inhibitor also downregulates levels and autophosphorylation (the addition of phosphate group) of Bcr-Abl, resulting in enhanced apoptosis of target cells when combined with the Bcr-Abl receptor tyrosine kinase inhibitor, compared to the treatment with either agent alone.

Dwg.0/3

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B07-D04C; B07-D11; B07-D12; B10-A18; B14-D06;
B14-D07; B14-H01; B14-H03;
B14-S09

ABEX UPTX: 20040505

SPECIFIC COMPOUNDS - **Imatinib** mesylate is specifically claimed as the tyrosine kinase inhibitor.
Suberoylanilide hydroxamic acid is specifically claimed as the histone deacetylase inhibitor.

ADMINISTRATION - The administration is for 48 hours (claimed). No dosage given.

EXAMPLE - No relevant example given.

L89 ANSWER 54 OF 54 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-558867 [52] WPIX
DOC. NO. NON-CPI: N2003-444359
DOC. NO. CPI: C2003-150507
TITLE: Identifying enzyme for designing anti-cancer compound, by selecting enzyme from genes and/or proteins whose expression level is more than two-fold in tumor tissue, as compared to normal cells or tissue.
DERWENT CLASS: B02 B03 B04 D16 S03
INVENTOR(S): ISHITSUKA, H; OKABE, H; SHIMMA, N; TSUKUDA, T; UMEDA, I
PATENT ASSIGNEE(S): (HOFF) HOFFMANN LA ROCHE & CO AG F; (CHUS) CHUGAI SEIYAKU KK; (ISHI-I) ISHITSUKA H; (OKAB-I) OKABE H; (SHIM-I) SHIMMA N; (TSUK-I) TSUKUDA T; (UMED-I) UMEDA I
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2003043631	A2	20030530	(200352)*	EN	118	A61K031-337	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU							
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK							
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR							
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT							
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW							
US 2003138864	A1	20030724	(200352)			G01N033-574	
AU 2002352048	A1	20030610	(200419)			A61K031-337	
EP 1492523	A2	20050105	(200504)	EN		A61K031-337	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC							
MK NL PT RO SE SI SK TR							
BR 2002014386	A	20041130	(200506)			A61K031-337	

NO 2004002609 A 20040622 (200513)

A61K031-337

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003043631	A2	WO 2002-EP12911	20021118
US 2003138864	A1	US 2002-301460	20021121
AU 2002352048	A1	AU 2002-352048	20021118
EP 1492523	A2	EP 2002-787721	20021118
		WO 2002-EP12911	20021118
BR 2002014386	A	BR 2002-14386	20021118
		WO 2002-EP12911	20021118
NO 2004002609	A	WO 2002-EP12911	20021118
		NO 2004-2609	20040622

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002352048	A1 Based on	WO 2003043631
EP 1492523	A2 Based on	WO 2003043631
BR 2002014386	A Based on	WO 2003043631

PRIORITY APPLN. INFO: EP 2002-5298 20020312; EP
 2001-127401 20011123; EP
 2001-130245 20011219

INT. PATENT CLASSIF.:

MAIN: A61K031-337; G01N033-574
 SECONDARY: A61K031-401; A61K031-4011; A61K031-426; A61K031-4266;
 A61K031-4725; A61K031-47255; A61K031-4745; A61K031-47455;
 A61K031-506; A61K031-5066; A61K031-513; A61K031-517;
 A61K031-5177; A61K031-53; A61K031-533; A61K031-704;
 A61K031-7044; A61K031-7068; A61K031-70688; A61K031-7072;
 A61K031-7076; A61K031-70766; C07D305-14; C07D405-02;
 C07D498-14; C07H019-48; C12Q001-68; C12Q001-688;
 G01N033-50; G01N033-500

BASIC ABSTRACT:

WO2003043631 A UPAB: 20030813

NOVELTY - Identifying (M1) an enzyme for designing an anti-cancer compound selectively converted to active substances in tumors, involves comparing the expression levels of genes and/or proteins in human tissue and/or cells from normal and tumor origin, and selecting an enzyme of which mRNA and/or protein levels in tumor tissue are higher by more than two-fold as compared to normal cells or tissue.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) use of enzyme identified by M1 for obtaining, identifying and/or designing anti-cancer compounds that can be converted to active substances selectively in tumors;

(2) identifying (M2) anti-cancer compounds that can be converted to active substances selectively in tumors, by generating cells expressing an enzyme of which protein levels in tumor tissue are higher by more than two-fold as compared to normal cells or tissue, and determining growth inhibitory activities of the anti-cancer compounds;

(3) anti-cancer prodrugs of formula X-Y-Q (I) or its salts;

(4) preparation of (I), where a compound Q-Y-H is condensed with a reactive derivative of X; and

(5) a pharmaceutical composition (PC) comprising (I).

X = pro-moiety that is designed to generate an active anti-cancer substance (Q-Y-H) selectively in tumors by the enzymes identified by M1;

Q = a radical derived from the active anti-cancer substance (Q-Y-H);
and

Y = -O-, -S- or -N-.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - Farnesyltransferase-Inhibitor; EGF-Receptor-Tyrosine-Kinase Inhibitor (claimed). No biological data is given.

USE - M1 is useful for identifying an enzyme (such as microsomal dipeptidase, arylsulfatase A, pyrroline 5'-carboxy reductase, dehydrodiol dehydrogenase, carbonyl reductase, lysyl hydroxylase, prolidase, dihydropyrimidinase, glutamine:fructose-6-phosphate amidotransferase, UDP-galactose ceramide galactosyl transferase, lysyl oxidase, enolase, glucose-6-phosphate dehydrogenase, steroyl-coenzyme A desaturase, epoxide hydrolase or aldolase C) for designing an anti-cancer compound that is selectively converted to active substances in tumors. (I) is useful for preparing medicaments for the treatment of cell proliferative disorders such as cancer, preferably colorectal, lung, breast, stomach, cervical or bladder cancer, or solid tumor, or in therapy. (I) is also useful for treating cell proliferative disorders (all claimed).

Dwg.0/0

FILE SEGMENT: CPI EPI

FIELD AVAILABILITY: AB; GI; DCN

MANUAL CODES: CPI: B02-D; B04-B03A; B04-L01; B06-H; B07-D03; B07-F01;
B11-C07A4; B11-C08E3; B12-K04A1; B12-K04F; B14-D06;
B14-H01; D05-H08; D05-H09; D05-H12A; D05-H12B;
D05-H13

EPI: S03-E14H5

TECH UPTX: 20030813

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The enzyme is identified by analyses of DNA microarray, PCR, Northern blotting and in situ hybridization, differential displays, RNase protection assay, protein arrays, Western blotting, two dimensional gel electrophoresis or enzyme-linked immunosorbent assay, preferably by analyses of DNA microarray or PCR. The normal cells or tissue are from hematopoietic progenitors derived from the bone marrow or umbilical cord blood, intestine, or skin. The human tissue and/or cells from tumor origin is from brain, lung, esophagus, breast, stomach, pancreas, liver, colon, rectum, kidney, ovary, uterus, bladder, prostate, skin and blood.

Preferred Compound: (I) is of formula (II), (III), (IV) or (V).

R0 = a side chain of natural or non-natural amino acid, preferably methyl, benzyl or 2-methylpropyl, cyclohexylmethyl, 2-naphtylmethyl, 4-phenylbenzyl, (4-cyclohexylcyclohexyl)methyl, alkylthiomethyl, cyclohexylthiomethyl or 4-alkoxybenzyl;

Z = 1-3C alkylene or -O-CH(R3)-;

R1 = H or methyl;

R2 = H, branched 3-10C alkyl or 3-8C cycloalkyl;

R3 = H or straight 1-4C alkyl;

Q- = a radical derived from the active anti-cancer substance (Q-Y-H) such as a taxane (such as taxol or taxotere), camptothecin (such as camptothecin or topotecan), anti-cancer nucleoside (such as decitabine or troxacitabine), dolastatin (such as dolastatin 10 or dolastatin 14), anthracycline (such as adriamycin or daunomycin), farnesyltransferase inhibitor (such as R-115777 of the formula 6-(1-amino-1-(4-chlorophenyl)-1-(1-methylimidazol-5-yl)methyl)-4-(3-chlorophenyl)-1-methylquinolin-2(1H)-one) or epidermal growth factor (EGF) receptor tyrosine kinase inhibitor (such as ZD 1839 having the formula N-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-(4-morpholinyl)propoxy)-4-quinazolinamine);

Y = -O-, -S- or -N-;

R4 = benzoyl or tert-butoxycarbonyl;

R5 = H or acetyl;
 R6 = H, fluorine, hydroxyl or cyano; and
 R7 = H, fluorine or hydroxy; or
 R6, R7 = methylenedioxy or fluoromethylenedioxy;
 R8 = H or ethynyl;
 R9 = H, fluorine, vinyl or ethynyl;
 R10 = H or hydroxy;
 m = 2 or 3;
 p = 1 to 3;
 n = 0 to 1;
 R11 = H or fluorine;
 R12 = H, fluorine, methyl or hydroxy;
 R13 = H, amino, nitro or (dimethylamino)methyl;
 R14 = H, 1-4C-alkyl, (4-methylpiperazinyl)methyl or (tert-butoxyimino)methyl; and
 R11, R12, R13, R14 = 5 or 6 membered ring which optionally contains 1 or 2 hetero atom(s) (optionally substituted with 1 to 3 substituent(s) selected from 1-8C alkyl, amino, 1-8C alkylamino and/or di-(1-4C)alkylamino).

ABEX

UPTX: 20030813

SPECIFIC COMPOUNDS - 3 compounds are specifically claimed as the taxol or taxotere (III), e.g. 13-((2R,3S)-2-((5S)-(5-((2S)-2-amino-4-methylpentanoylamino)-5-hydroxycarbonyl)pentanoyloxy)-3-benzoylamino-3-phenylpropionyloxy)-2- α -benzyloxy-4- α ,10- β -diacetoxy-1- β ,7- β -dihydroxy-5- β ,20-epoxy-tax-11-en-9-one (IIIa). 18 compounds are specifically claimed as the anticancer nucleoside (IV), e.g. (2R)-((2S)-amino-3-cyclohexyl-propionylamino)-(3S)-(1-((4S)-hydroxy-(5R)-hydroxymethyl-3-methylene-tetrahydro-furan-(2R)-yl)-2-oxo-1,2-dihydropyrimidine-4-yl-carbamoyloxy)-butyric acid (IVa). 53 compounds are specifically claimed as the camptothecin or its derivative (V), e.g. 20-O-((S)-tryptophyl-gamma-(S)-glutamyl)-20-(S)-camptothecin (Va).

ADMINISTRATION - The composition is administered by oral or parenteral route (claimed) at a dose of 5-500 mg/m². The composition can also be administered by rectal route.

EXAMPLE - Selection of the enzymes that are expressed preferably in tumors but not in granulocyte progenitors and liver was as follows. CD-positive mononuclear cells derived from the human umbilical cord blood and bone marrow were obtained and were cultured on a confluent monolayer of MS5 mouse stromal cell lines in α modified Eagle medium (MEM) medium supplemented with 10% (v/v) horse serum (HS), 10% (v/v) fetal bovine serum (FBS), Flt3 ligand (50 ng/ml), SCF (100 ng/ml), and TPO (50 ng/ml), at 37 degreesC under 5% CO₂ in humidified air. Floating hematopoietic cells were collected and stained by monoclonal antibodies against PerCP-anti-CD34, PE-anti-CD13 and fluorescein isothiocyanate (FITC)-anti-15. 5 microl of each antibody was added to a 50 l of cell suspension and incubated at 4 degreesC for 25 minutes. After washing with phosphate buffered saline (PBS) containing 10% (v/v) fetal calf serum (FCS), the expression of CD antigens were detected by using fluorescence activated cell sorting (FACS) Calibur. FACS analysis revealed that more than 90% of mononuclear cells preexpressed CD34 progenitor marker after they were expanded in the above condition. When these CD34-positive cells were treated with 50 ng/ml of granulocyte-colony stimulating factor (G-CSF), more than 80% of the cells were differentiated into CD34-negative, CD13- and CD15-positive myeloblasts and myelocytes within 7 days and further into neutrophils within 14 days after addition of G-CSF. DNA chip experiments yielded several hundreds cDNAs of which mRNA was considered to be absent or expressed only at very low levels. In granulocyte progenitors and liver, but was expressed at certain levels in tumors of breast, liver, gastric, colorectum, pancreas, or ovary in more than 50% of the patients. Among

such cDNAs, more than 150 cDNAs that encoded proteins possessing a known catalytic activity were selected. Those enzymes include phospholipase C, microsomal dipeptidase, arylsulfatase A, DT-diaphorase, pyrroline 5'-carboxy reductase, dehydrodiol dehydrogenase, carbonyl reductase, lysyl hydroxylase, prolidase, dihydropyrimidinase, gamma-glutamyl transpeptidase, glutamine:fructose-6-phosphate amidotransferase, UDP-galactose ceramide galactosyl transferase, lysyl oxidase, enolase, glucose-6-phosphate dehydrogenase, uridine phosphorylase, steroyl-coenzyme desaturase, epoxide hydrolase, aldolase C.

DEFINITIONS - Preferred Definition:

Q = a taxane (such as taxol or taxotere), camptothecin (such as camptothecin or topotecan), anti-cancer nucleoside (such as decitabine or **troxacitabine**), dolastatin (such as dolastatin 10 or dolastatin 14), anthracycline (such as adriamycin or daunomycin), farnesyltransferase inhibitor (such as R-115777 of the formula 6-(1-amino-1-(4-chlorophenyl)-1-(1-methylimidazol-5-yl) methyl)-4-(3-chlorophenyl)-1-methylquinolin-2(1H)-one) or epidermal growth factor (EGF) receptor **tyrosine kinase** inhibitor (such as ZD 1839 having the formula N-(3-chloro-4-fluorophenyl)-7-methoxy- 6-(3-(4-morpholinyl)propoxy)-4-quinazolinamine).

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RECORDS LAST ADDED: 9 March 2005 (20050309/ED)

FILE RELOADED: 19 October 2003.

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ON STANDARD TERMS USED IN DSM-IV (DIAGNOSTIC AND
STATISTICAL MANUAL OF MENTAL DISORDERS - FOURTH
EDITION).

FOR FURTHER DETAILS:

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=> d his l88

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16 MAR 2005)

L88 13 S L87 AND (L14 OR L63 OR L41 OR L12)

=> d que 188

L12 QUE ABB=ON PLU=ON STI(1W)571
L14 QUE ABB=ON PLU=ON ?TYROSIN?(2A)?KINAS?
L41 QUE ABB=ON PLU=ON ?IMATINIB?
L62 QUE ABB=ON PLU=ON (?TROXACITABIN? OR ?TROXATYL? OR (SP
 D(1W)758) OR OCCC OR (BCH(1W)(204 OR 4556)) OR (?DIOXALAN
 ?(1W)C))
L63 QUE ABB=ON PLU=ON ((CGP(1W)57148B) OR ?GLEEVAC? OR ?GL
 EEVEC? OR ?GLIVEC?)
L83 2352 SEA GILES, F?/AU
L84 609 SEA VERSTOVSEK, S?/AU
L85 120 SEA (L83 OR L84) AND L62
L86 55 DUP REM L85 (65 DUPLICATES REMOVED)
L87 52 SEA (?CANCER? OR ?CARCIN? OR ?NEOPLAS? OR ?LEUK? OR ?ONCOLO?
 OR ?PROLIFER? OR ?TUMOR? OR ?TUMOUR?) AND L86
L88 13 SEA L87 AND (L14 OR L63 OR L41 OR L12)

=> d ibib ed ab l88 1-

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CONTINUE? (Y)/N:y

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L88 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:334928 HCAPLUS

DOCUMENT NUMBER: 140:399534

TITLE: **Troxacitabine and imatinib**
mesylate combination therapy of chronic myeloid
leukaemia: preclinical evaluation

AUTHOR(S): Orsolic, Nada; **Giles, Francis J.**; Gourdeau,
Henriette; Golemovic, Mirna; Beran, Miloslav; Cortes,
Jorge; Freireich, Emil J.; Kantarjian, Hagop;
Verstovsek, Srdan

CORPORATE SOURCE: Department of Leukemia, M.D. Anderson Cancer Center,
The University of Texas, Houston, TX, USA

SOURCE: British Journal of Haematology (2004), 124(6), 727-738
CODEN: BJHEAL; ISSN: 0007-1048

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 25 Apr 2004

AB The in vitro and in vivo activity of a deoxycytidine analog,
troxacitabine, alone or in combination with **imatinib**
mesylate (IM), was evaluated against human chronic myeloid
leukemia (CML) cell lines both sensitive (KBM5 and KBM7) and
resistant (KBM5-R and KBM7-R) to IM. These cell lines differ in their
sensitivity to IM but all showed similar sensitivity to treatment with
troxacitabine (IC50 = 0.5-1 µmol/l). Combined treatment with
troxacitabine and IM revealed additive or synergistic effects.
Greater apoptotic response was seen with, combined treatment than with
either agent alone in KBM7-R cells. In clonogenic assays,
troxacitabine showed activity against mononuclear cells from CML
patients (IC50 = 0.01 µmol/l) with either IM-sensitive or resistant
disease. In vivo efficacy studies were carried out in severe combined
immunodeficient mice bearing KBM5 or KBM5-R cells. **Troxacitabine**
was administered i.p. daily for 5 d starting on day 20, at doses of 5, 10,
20, or 25 mg/kg. IM was administered i.p. twice a day for 10 d at a dose
of 50 mg/kg starting on day 25. In this setting of late stage disease,
troxacitabine led to a significant increase in life span, while IM
did not. When IM was combined with **troxacitabine** at 10 and 25
mg/kg in the KBM5 xenograft model, a further increase in life span was
observed and some mice achieved long-term survival. These data indicate that
the combination of **troxacitabine** and IM has significant preclin.
activity in advanced CML and that clin. evaluation of this combination is
warranted.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS
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L88 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:997599 HCAPLUS

DOCUMENT NUMBER: 140:12393

TITLE: New agents in chronic myelogenous leukemia

AUTHOR(S): Cortes, Jorge; **Giles, Francis**

CORPORATE SOURCE: Department of Leukemia, M. D. Anderson Cancer Center,
The University of Texas, Houston, TX, USA

SOURCE: Journal of the National Comprehensive Cancer Network
(2003), 1(4), 501-512
CODEN: JNCCA4; ISSN: 1540-1405
PUBLISHER: Jones and Bartlett Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 23 Dec 2003
AB A review. Multiple new agents are currently being developed in chronic myelogenous leukemia (CML). Most of these agents are now being investigated in patients who have developed resistance to **imatinib**. Their mechanisms of action are diverse and many may be synergistic with **imatinib**. These agents will be used soon in different combinations, most likely including **imatinib**, with the hope of obtaining a complete blockade of the intracellular pathways that are triggered by Bcr-Abl. If this is successful, complete eradication of disease may become a reality for the majority of patients with CML.
REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:621850 HCAPLUS
DOCUMENT NUMBER: 140:228562
TITLE: Phase II study of **troxacitabine**, a novel dioxolane nucleoside analog, in patients with untreated or **imatinib** mesylate-resistant chronic myelogenous leukemia in blastic phase
AUTHOR(S): Giles, Francis J.; Feldman, Eric J.; Roboz, Gail J.; Larson, Richard A.; Mamus, Steven W.; Cortes, Jorge E.; Verstovsek, Srdan; Faderl, Stefan; Talpaz, Moshe; Beran, Miloslav; Albitar, Maher; O'Brien, Susan M.; Kantarjian, Hagop M.
CORPORATE SOURCE: M.D. Anderson Cancer Center, Department of Leukemia, University of Texas, Houston, TX, 77030, USA
SOURCE: Leukemia Research (2003), 27(12), 1091-1096
CODEN: LEREDD; ISSN: 0145-2126
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 13 Aug 2003
AB A phase II study of **troxacitabine**, a non-natural dioxolane nucleoside L-enantiomer, was conducted in patients with chronic myelogenous leukemia in blastic phase (CML-BP). Patients were untreated for BP, or treated with **imatinib** mesylate (IM) as sole prior therapy for BP. **Troxacitabine** was given as an i.v. infusion over 30 min daily for 5 days at a dose of 8.0 mg/m² per day. Thirty-one patients, 29 (93%) of whom had failed prior IM therapy, received 51 courses of therapy. Grade 3 or 4 toxicities included stomatitis (4%), hand-foot syndrome (18%), and skin rash (12%). Four patients (13%) responded. **Troxacitabine**-based combinations merit study in IM-resistant CML.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:356264 HCAPLUS
DOCUMENT NUMBER: 138:348696
TITLE: Pharmaceutical compositions for the treatment of leukemia comprising dioxolane nucleosides

INVENTOR(S): analogs
Jolivet, Jacques; Giles, Francis J.;
Kantarjian, Hagop
PATENT ASSIGNEE(S): Shire Biochem Inc., Can.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037344	A1	20030508	WO 2002-CA1687	20021104
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003125305	A1	20030703	US 2002-286960	20021104
<u>US 6645972</u>	B2	20031111		
EP 1441733	A1	20040804	EP 2002-771956	20021104
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
PRIORITY APPLN. INFO.:			US 2001-330891P	P 20011102
			WO 2002-CA1687	W 20021104

OTHER SOURCE(S): MARPAT 138:348696

ED Entered STN: 09 May 2003

AB The present invention provides a novel method for treating **leukemia** in a host that has been previously treated with a Bcr-Abl **tyrosine kinase** inhibitor comprising administering to the host a therapeutically effective amount of a dioxolane nucleoside analog.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L88 ANSWER 5 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2004043980 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14745859
TITLE: New agents in acute myeloid **leukemia** and other myeloid disorders.
AUTHOR: Ravandi Farhad; Kantarjian Hagop; Giles Francis; Cortes Jorge
CORPORATE SOURCE: Department of Leukemia, The University of Texas M D Anderson Cancer Center, Houston, Texas 77030, USA.. fravandi@mdanderson.org
SOURCE: Cancer, (2004 Feb 1) 100 (3) 441-54. Ref: 140
Journal code: 0374236. ISSN: 0008-543X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200402

ENTRY DATE: Entered STN: 20040128
Last Updated on STN: 20040220
Entered Medline: 20040219

ED Entered STN: 20040128

Last Updated on STN: 20040220

Entered Medline: 20040219

AB Over the past several decades, improvements in chemotherapeutic agents and supportive care have resulted in significant progress in treating patients with acute myeloid **leukemia** (AML). More recently, advances in understanding the biology of AML have resulted in the identification of new therapeutic targets. The success of all-trans-retinoic acid in acute promyelocytic **leukemia** and of **imatinib** mesylate in chronic myeloid **leukemia** have demonstrated that targeted therapy may be more effective and less toxic when well defined targets are available. At the same time, understanding mechanisms of drug resistance and means to overcome them has led to modification of some of the existing cytotoxic agents. Rational design and conduct of clinical trials is necessary to ensure that the full potential of these new agents is realized.

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ACCESSION NUMBER: 2002:152475 BIOSIS

DOCUMENT NUMBER: PREV200200152475

TITLE: Phase II study of **Troxatyl**TM in patients with chronic myeloid **leukemia** in blastic phase (CML-BP).

AUTHOR(S): Giles, Francis [Reprint author]; Feldman, Eric; Cortes, Jorge [Reprint author]; Faderl, Stefan [Reprint author]; Larson, Richard; Mamus, Steven; Thomas, Deborah [Reprint author]; Garcia-Manero, Guillermo [Reprint author]; O'Brien, Susan [Reprint author]; Beran, Milsolav [Reprint author]; Talpaz, Moshe [Reprint author]; Kantarjian, Hagop [Reprint author]

CORPORATE SOURCE: UT MD Anderson Cancer Center, Houston, TX, USA

SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 258b. print.

Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Feb 2002

Last Updated on STN: 26 Feb 2002

ED Entered STN: 21 Feb 2002

Last Updated on STN: 26 Feb 2002

AB **Troxatyl** triphosphate (converted by the intracellular phosphorylation of **Troxatyl**) is a potent inhibitor and chain terminator for human cellular DNA polymerases and was a unique pattern of cellular uptake and metabolism. On a Phase I study, **Troxatyl** had significant **antileukemia** activity in patients with refractory disease. (Giles et al, JCO: 19:762:2001). The recommended single agent dose was defined as 8 mg/m²/day daily for 5 days. On a subsequent Phase II study, 6 patients with CML-BP of 16 evaluable (37%) achieved a return to chronic phase disease. (Giles et al, JCO: In press). Three of the 6 responding patients received **Troxatyl** as first therapy for CML-BP; one patient had failed STI571 as prior sole therapy for CML-BP. A multicenter Phase II study of **Troxatyl** 8

mg/m²/day daily for 5 days for patients with CML-BP who have received no prior chemotherapy for CML-BP is being conducted. Patients who have received Gleevec therapy as sole prior therapy for CML-BP are also eligible. Twenty-six patients, 17 male, 26 performance score ltoreq2, median age 54 years (range 31-84) have been entered on study to date, 13 (50%) patients received Troxatyl as first therapy for CML-BP, 13 (50%) had failed prior Gleevec therapy for CML-BP. Response definitions are as follows: Complete hematologic response (CHR) requires normalization of peripheral counts and differentials with ltoreq5% marrow blasts for at least 4 weeks. Hematologic improvement (HI) is as with CHR but with persistence of thrombocytopenia less than 100X10⁹/L and few immature peripheral cells. A partial hematologic response (PHR) is as per CHR, but allows persistence of, though gtoreq50% reduction of, palpable splenomegaly and thrombocytosis (platelets>450X10⁹/L), or the presence of few immature peripheral cells. Back to second chronic phase (BCP) requires disappearance of BP features and return to chronic phase CML features, i.e., peripheral blasts <15%, peripheral blasts+promyelocytes <30%, peripheral basophils <20%, and platelets >100X10⁹/L. In patients with extramedullary disease (EMD), complete response (CR) requires CHR plus disappearance of all EMD. PR in patients with EMD require at least a 50% reduction in all EMD. Twenty-one patients who have received a total of 40 cycles (range 1 to 4) of Troxatyl therapy are currently evaluable for response - 1 PR, 1 HI, 1 BCP, and 1 CR in a patient with EMD have been recorded to date. Four patients died during cycle 1 of therapy - one with a CVA, 3 with sepsis/progressive disease. Extramedullary grade 3 or 4 attributable adverse events in the first cycle of therapy included skin rash (3), hyperbilirubinemia (3), hand foot syndrome (1), colitis (1). One patient developed Sweets Syndrome during 1st cycle of therapy - this subsequently completely resolved. Median survival in the study cohort is 9 months with 33% of patients alive at 1 year. Troxatyl has significant activity in patients with CML-BP. Accrual continues on this study.

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ACCESSION NUMBER: 2004318012 EMBASE
TITLE: Accelerated and blastic phases of chronic myelogenous leukemia.
AUTHOR: Giles F.J.; Cortes J.E.; Kantarjian H.M.; O'Brien S.M.
CORPORATE SOURCE: Dr. F.J. Giles, Department of Leukemia, The University of Texas, M.D. Anderson Cancer Ctr., 1515 H., Houston, TX, United States. fgiles@mdanderson.org
SOURCE: Hematology/Oncology Clinics of North America, (2004) 18/3 (753-774).
Refs: 177
ISSN: 0889-8588 CODEN: HCNAEQ
PUBLISHER IDENT.: S 0889-8588(04)00010-3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although the mechanisms of CML transformation remain poorly understood, recent therapeutic advances moderately have improved the prognosis of patients in AP and BP. Treatment with IFN- α -based regimens are minimally effective for patients in AP and ineffective for those in BP.

Imatinib mesylate has a significant but generally transient response rate in patients in AP and BP. Hope for progress in this area lies mainly in the development of novel targeted therapies. The more promising agents that are being investigated include decitabine, HHT, **troxacitabine**, clofarabine, farnesyl transferase inhibitors, histone deacetylase inhibitors, and the VEGF and mTOR inhibitors. Many of these approaches may be synergistic with **imatinib** or the more powerful abl or Src inhibitors that are in development.

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ACCESSION NUMBER: 2004165534 EMBASE
TITLE: Novel therapies for patients with chronic myeloid leukemia.
AUTHOR: Giles F.J.; Kantarjian H.; Cortes J.
CORPORATE SOURCE: Dr. F.J. Giles, Department of Leukemia, University of Texas, MD Anderson Cancer Center, 1400 Holcombe Boulevard, Houston, TX 77030, United States. frankgiles@aol.com
SOURCE: Expert Review of Anticancer Therapy, (2004) 4/2 (271-282).
Refs: 177
ISSN: 1473-7140 CODEN: ERATBJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The most immediate issues that will have a major impact on the long-term survival of patients with chronic myeloid leukemia is the optimal use of **imatinib** mesylate (Gleevec.RTM., Novartis) and the development of effective therapies for those patients who are intolerant of, or become resistant to, optimal doses of this agent. Of the multiple new agents that are currently being developed for patients with chronic myeloid leukemia, most are being investigated in patients who have developed resistance to **imatinib**, which is a confounding factor in itself. The mechanisms of action of novel agents are diverse and they may have a variably synergistic therapeutic relationship with **imatinib**. The complete blockade of the intracellular pathways that are triggered by Bcr-Abl, combined with successful reversal of apoptotic and/or angiogenic abnormalities in chronic myeloid leukemia, may well lead to a cure for the majority of patients. .COPYRG. Future Drugs Ltd. All rights reserved.

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ACCESSION NUMBER: 2003396846 EMBASE
TITLE: Phase 2 clinical and pharmacologic study of clofarabine in patients with refractory or relapsed acute leukemia
AUTHOR: Kantarjian H.; Gandhi V.; Cortes J.; Verstovsek S.; Du M.; Garcia-Manero G.; Giles F.; Faderl S.; O'Brien S.; Jeha S.; Davis J.; Shaked Z.; Craig A.; Keating M.; Plunkett W.; Freireich E.J.
CORPORATE SOURCE: H. Kantarjian, Department of Leukemia, Box 428, Univ. Texas MD Anderson Cancer Ctr., 1515 Holcombe Blvd, Houston, TX 77030, United States. hkantarj@mdanderson.org
SOURCE: Blood, (1 Oct 2003) 102/7 (2379-2386).

Refs: 40
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In a phase 2 study, 62 patients with relapsed and refractory acute myeloid leukemia (AML; n = 31), myelodysplastic syndrome (MDS; n = 8), chronic myeloid leukemia in blastic phase (CMLBP; n = 11), and acute lymphocytic leukemia (ALL; n = 12) received 40 mg/m² clofarabine intravenously over 1 hour daily for 5 days, every 3 to 6 weeks. Twenty patients (32%) achieved complete response (CR), 1 had a partial response (PR), and 9 (15%) achieved CR but without platelet recovery (CRp), for an overall response rate of 48%. In AML, responses were noted in 2 (18%) of 11 patients in first salvage with short first CR (≤ 12 months), in 7 (87%) of 8 patients with longer first CR, and in 8 (67%) of 12 patients in second or subsequent salvage. Responses were observed in 4 of 8 patients with high-risk MDS (50%), in 7 (64%) of 11 with CML-BP, and in 2 (17%) of 12 with ALL. Severe reversible liver dysfunction was noted in 15% to 25%. After the first clofarabine infusion, responders accumulated more clofarabine triphosphate in blasts compared with nonresponders (median 18 vs 10 μ M; $P = .03$). This increased only in responders (median, 1.8-fold; $P = .008$) after the second clofarabine infusion. In summary, clofarabine is active in acute leukemias and MDS; cellular pharmacokinetics may have prognostic significance.
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L88 ANSWER 10 OF 13 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-10803 DRUGU P
TITLE: Troxatyl and STI571 combination therapy for chronic myeloid leukemia: preclinical in vitro and in vivo evaluation.
AUTHOR: Orsolic N; Giles F; Beran M; Cortes J; Albitar M; Kantarjian H; Verstovsek S
CORPORATE SOURCE: Univ.Texas-Syst.
LOCATION: Houston, Tex., USA
SOURCE: Blood (100, No. 11, Pt. 1, 786a, 2002) 2 Ref.
CODEN: BLOOAW ISSN: 0006-4971
AVAIL. OF DOC.: Leukemia, The University of Texas, MD Anderson Cancer Center, Houston, TX, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The effects of Troxatyl (TX, troxycitabine) and imatinib (IM, STI-571) were investigated in-vitro in chronic myeloid leukemia (CML) KBM5 and KBM7 cells, IM-resistant sublines KBM5-R and KBM7-R, cells from patients with CML and in-vivo after i.p. administration in mice bearing KBM5 or KBM5-R cells. TX and IM showed a synergistic cytostatic activity both in in-vitro and in-vivo studies. In conclusion, the results show that TX has activity in late stage CML and that combining it with IM is a very reasonable clinical approach. (conference abstract: 44th Annual Meeting of the American Society of Hematology, Philadelphia, Pennsylvania, USA, 2002).

L88 ANSWER 11 OF 13 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-17334 DRUGU T S
TITLE: Phase II study of **Troxatyl** in patients with chronic myeloid leukemia in blastic phase (CML-BP).
AUTHOR: **Giles F**; Feldman E; Cortes J; Faderl S; Larson R; Mamus S; Thomas D; Garcia Manero G; O'Brien S; Beran M; Talpaz M; Kantarjian H
CORPORATE SOURCE: Anderson-Cancer-Cent.; Univ.Chicago; Univ.Cornell
LOCATION: Houston, Tex., New York, N.Y., Chicago, Ill.; Orlando, Fla., USA
SOURCE: Blood (98, No. 11, Pt. 2, 258b, 2001) 1 Ref.
CODEN: BLOOAW ISSN: 0006-4971
AVAIL. OF DOC.: UT MD Anderson Cancer Center, Houston, TX, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The efficacy of **troxacitabine (Troxatyl)** was investigated in 26 patients with chronic myeloid leukemia in blastic phase (CML-BP) in a phase II study. Side-effects included skin rash, hyperbilirubinemia, hand foot syndrome, colitis, and Sweets syndrome. The result showed that **Troxatyl** had significant activity in these CML-BP patients. (conference abstract: 43rd Annual Meeting of the American Society of Hematology, Orlando, Florida, USA, 2001).

L88 ANSWER 12 OF 13 DRUGU COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-12589 DRUGU T S
TITLE: **Troxatyl** is effective in non-lymphoid blastic phase chronic myeloid leukemia (CML-BP).
AUTHOR: **Giles F**; Talpaz M; Bivins C; Jolivet J; Kantarjian H
CORPORATE SOURCE: Univ.Texas-Syst.
LOCATION: Houston, Tex., USA
SOURCE: Eur.J.Cancer (37, Suppl. 6, S35, 2001) 2 Ref.
CODEN: EJCAEL ISSN: 0964-1947
AVAIL. OF DOC.: University of Texas MD Anderson Cancer Center, Houston, TX, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The use of **troxacitabine (Troxatyl)** to treat 17 patients with non-lymphoid blastic phase chronic myeloid leukemia (CML-BP) is reported. Side-effects included rash, hand-foot syndrome and mucositis. Median survival was over 52 wk. **Troxatyl** as a single agent in CML-BP is under study in Phase II trial. (conference abstract: 11th European Cancer Conference, Lisbon, Portugal, 2001).

L88 ANSWER 13 OF 13 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-480817 [45] WPIX
DOC. NO. CPI: C2004-178848
TITLE: Combination, useful for the treatment of leukemia e.g. acute myelogenous leukemia and chronic myelogenous leukemia, comprises isoxazole derivatives and a Bcr-Abl tyrosine kinase inhibitor.
DERWENT CLASS: B03
INVENTOR(S): GILES, F J; VERSTOVSEK, S

PATENT ASSIGNEE(S): (GILE-I) GILES F J; (VERS-I) VERSTOVSEK S; (SHIR-N) SHIRE
 BIOCHEM INC
 COUNTRY COUNT: 106
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004052369	A1	20040624	(200445)*	EN	55
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2004192652	A1	20040930	(200465)		
AU 2003291882	A1	20040630	(200472)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004052369	A1	WO 2003-CA1909	20031208
US 2004192652	A1 Provisional	US 2002-431196P	20021206
		US 2003-729387	20031208
AU 2003291882	A1	AU 2003-291882	20031208

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003291882	A1 Based on	WO 2004052369
PRIORITY APPLN. INFO: US 2002-431196P		20021206; US
2003-729387		20031208

ED 20040716

AB WO2004052369 A UPAB: 20040716

NOVELTY - Pharmaceutical combination (A) comprises isoxazole derivatives (I) and their salts and a Bcr-Abl tyrosine kinase inhibitor (B).

DETAILED DESCRIPTION - Pharmaceutical combination (A) comprises isoxazole derivatives of formula (I) and their salts and a Bcr-Abl tyrosine kinase inhibitor (B).

B = cytosine or 5-fluorocytosine;

R = H, mono-tri phosphate, carbonyl substituted with 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 6-10C aryl or -P(O)2ORc; and

Rc = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl or hydroxy protecting group.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Tyrosine kinase inhibitor.

USE - (A) is useful for the treatment of leukemia e.g. acute myelogenous leukemia, chronic myelogenous leukemia in blastic phase, refractory/relapsed leukemia and chronic myelogenous leukemia.

ADVANTAGE - (A) has synergistic effect to reduce the leukemia

The effect of (A) in treating leukemia was assessed using an in vivo study in mice. The results showed that the combination of Troxatyl with STI-571 provided a synergistic effect in treating leukemia.

Dwg.0/14

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FILE 'STNGUIDE' ENTERED AT 13:33:13 ON 16 MAR 2005

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Mar 11, 2005 (20050311/UP).

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